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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  DEC 05  CASREACT(R) - Over 10 million reactions available
 NEWS  4  DEC 14  2006 MeSH terms loaded in MEDLINE/LMEDLINE
 NEWS  5  DEC 14  2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
 NEWS  6  DEC 14  CA/CAplus to be enhanced with updated IPC codes
 NEWS  7  DEC 21  IPC search and display fields enhanced in CA/CAplus with the
                  IPC reform
 NEWS  8  DEC 23  New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                  USPAT2
 NEWS  9  JAN 13  IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS 10  JAN 13  New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                  INPADOC
 NEWS 11  JAN 17  Pre-1988 INPI data added to MARPAT
 NEWS 12  JAN 17  IPC 8 in the WPI family of databases including WPIFV
 NEWS 13  JAN 30  Saved answer limit increased
 NEWS 14  JAN 31  Monthly current-awareness alert (SDI) frequency
                  added to TULSA
 NEWS 15  FEB 21  STN AnaVist, Version 1.1, lets you share your STN AnaVist
                  visualization results
 NEWS 16  FEB 22  Status of current WO (PCT) information on STN
 NEWS 17  FEB 22  The IPC thesaurus added to additional patent databases on STN
 NEWS 18  FEB 22  Updates in EPFULL; IPC 8 enhancements added
 NEWS 19  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS 20  FEB 28  MEDLINE/LMEDLINE reload improves functionality
 NEWS 21  FEB 28  TOXCENTER reloaded with enhancements
 NEWS 22  FEB 28  REGISTRY/ZREGISTRY enhanced with more experimental spectral
                  property data
 NEWS 23  MAR 01  INSPEC reloaded and enhanced
 NEWS 24  MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 10:36:34 ON 06 MAR 2006

=> file uspatful
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'USPATFULL' ENTERED AT 10:36:47 ON 06 MAR 2006
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Mar 2006 (20060302/PD)
FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)
HIGHEST GRANTED PATENT NUMBER: US7007305
HIGHEST APPLICATION PUBLICATION NUMBER: US2006048257
CA INDEXING IS CURRENT THROUGH 28 Feb 2006 (20060228/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Mar 2006 (20060302/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005


=> e grogan c c/in
E1            1      GROFT WILLIAM E/IN
E2            1      GROFTE THORBJORN/IN
E3            0 -->  GROGAN C C/IN
E4            1      GROGAN CASE C/IN
```

```
E6          3     GROGAN CHARLES W/IN
E7          4     GROGAN DANIEL/IN
E8          1     GROGAN DANIEL R/IN
E9          1     GROGAN DANIEL W/IN
E10         1     GROGAN DARREN/IN
E11         2     GROGAN DENISE C/IN
E12         1     GROGAN DENNIS/IN

=> s e4
L1          1 "GROGAN CASE C"/IN

=> d l1,cbib,ab,clm
```

L1 ANSWER 1 OF 1 USPATFULL on STN
2003:158947 Chimeric filovirus glycoprotein.

Grogan, Case C., Gaithersburg, MD, UNITED STATES
Hevey, Michael C., Frederick, MD, UNITED STATES
Schmaljohn, Alan L., Frederick, MD, UNITED STATES
US 2003108560 A1 20030612
APPLICATION: US 2002-66506 A1 20020131 (10)
PRIORITY: US 2001-267522P 20010131 (60)
DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Chimeric GP molecules were constructed which contain portions of both the EBOV and MBGV GP proteins by swapping the subunits between EBOV and MBGV. The chimeric molecules were cloned into an alphavirus replicon which offers the advantage of high protein expression levels in mammalian cells and is a proven vaccine vector. These chimeric molecules fully protected guinea pigs from MBGV challenge, and conversely protected the animals from EBOV challenge. These results indicate that a protective epitope resides within the GP2 subunit of the MBGV GP protein and at least partially within the GP2 subunit of the EBOV GP protein. Additionally these results show that a construction of a single-component bivalent vaccine protective in guinea pigs is achievable.

CLM What is claimed is:

1. A chimeric filovirus GP protein comprising GP1 and GP2 wherein said GP1 is chosen from a filovirus different than that of GP2.

2. The chimeric filovirus GP protein according to claim 1 wherein said GP1 or GP2 is from a filovirus chosen from the Genera consisting of Ebola and Marburg.

3. The chimeric filovirus GP protein according to claim 2 wherein said Ebola is chosen from the species Zaire, Sudan, Reston, and Cote d'Ivoire.

4. The chimeric filovirus GP protein according to claim 2 wherein said Marburg is chosen from the species Musoke, Ravn, and Popp.

5. The chimeric filovirus GP protein according to claim 1 wherein said GP1 is from Ebola and GP2 is from Marburg.

6. The chimeric filovirus GP protein according to claim 5 wherein said Ebola is strain Zaire and said Marburg is strain Musoke.

7. The chimeric filovirus GP protein according to claim 1 wherein said GP1 is from Marburg and GP2 is from Ebola.

8. The chimeric filovirus GP protein according to claim 7 wherein said Marburg is strain Musoke and said Ebola is strain Zaire.

9. The chimeric filovirus GP protein according to claim 1 wherein said GP1 is from Marburg strain Musoke and said GP2 is from Marburg strain Ravn.

10. The chimeric filovirus GP protein according to claim 1 wherein said GP1 is from Marburg strain Ravn and said GP2 is from Marburg strain Musoke.

11. The chimeric filovirus GP protein according to claim 6 wherein said chimeric GP is EBGP1/MBGP2 identified in SEQ ID NO:2 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

12. A DNA fragment encoding the chimeric protein of claim 11, said DNA identified in SEQ ID NO:1 and conservative substitutions thereof.

13. The chimeric filovirus GP protein according to claim 8 wherein said chimeric GP is MBGP1/EBGP2 identified in SEQ ID NO:4 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

14. A DNA fragment encoding the chimeric protein of claim 13, said DNA identified in SEQ ID NO:3.

15. The chimeric filovirus GP protein according to claim 9 wherein said chimeric GP is MUSGP1/RVNGP2 identified in SEQ ID NO:6 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

16. A DNA fragment encoding the chimeric protein of claim 15, said DNA identified in SEQ ID NO:5.

17. The chimeric filovirus GP protein according to claim 10 wherein said chimeric GP is RVNGP1/MUSGP2 identified in SEQ ID NO:8 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

18. A DNA fragment encoding the chimeric protein of claim 17, said DNA identified in SEQ ID NO:7.

19. A recombinant DNA construct comprising: (i) a vector, and (ii) a DNA fragment encoding a chimeric filovirus GP protein according to claim 1.

20. The recombinant DNA construct according to claim 19 wherein said DNA fragment encodes any of the following chimeric proteins chosen from the group consisting of: (i) Marburg Musoke GP1/Ebola Zaire GP2 (ii) Ebola Zaire GP1/Marbug Musoke GP2 (iii) Marburg Musoke GP1/Marburg Ravn GP2 (iv) Marburg Ravn GP1/Marburg Musoke GP2

21. A recombinant DNA construct according to claim 20 wherein said vector is an expression vector.

22. A recombinant DNA construct according to claim 20 wherein said vector is a prokaryotic vector.

23. A recombinant DNA construct according to claim 20 wherein said vector is a eukaryotic vector.

24. A recombinant DNA construct according to claim 20 wherein said vector is a VEE virus replicon vector.

25. The recombinant DNA construct according to claim 24 wherein said construct is EBOV-MAY SP1 (aa1-501)/MBGV-MUS GP2 (aa436-681).

26. The recombinant DNA construct according to claim 24 wherein said construct is MBGV-MUD GP1 (aa1-435)/EBOV-MAY GP2 (aa502-676).

27. The recombinant DNA construct according to claim 24 wherein said construct is MBGV-RVN GP1 (aa1-435)/MBGV-MUS GP2 (aa436-681).

28. The recombinant DNA construct according to claim 24 wherein said construct is MBGV-MUS GP1 (aa1-435)/MBGV-RVN GP2 (aa436-681).

29. Self replicating RNA produced from the construct of any of claims 24-28.

30. Infectious alphavirus particles produced from packaging the self replicating RNA of claim 29.

31. A pharmaceutical composition comprising infectious alphavirus particles according to claim 30 in an effective immunogenic amount in a pharmaceutically acceptable carrier and/or adjuvant.

32. A host cell transformed with a recombinant DNA construct according to claim 19.

33. A host cell according to claim 32 wherein said host cell is prokaryotic.

34. A host cell according to claim 32 wherein said host cell is eukaryotic.

35. A method for producing chimeric filovirus GP proteins comprising culturing the cells according to claim 33 under conditions such that said DNA fragment is expressed and said chimeric protein is produced.

36. A method for producing chimeric filovirus GP proteins comprising culturing the cells according to claim 34 under conditions such that said DNA fragment is expressed and said chimeric protein is produced.

37. A vaccine for more than one filovirus comprising viral particles containing one or more replicon RNA encoding chimeric GP from one or

38. A vaccine against Ebola Zaire virus infection and Marburg Musoke virus infection comprising a chimeric GP protein according to claim 5.

39. A vaccine against Ebola Zaire virus infection and Marburg Musoke virus infection comprising a chimeric GP protein according to claim 7.

40. A vaccine against Marburg Musoke virus infection and Marburg Ravn virus infection comprising a chimeric GP protein according to claim 9.

41. A vaccine against Marburg Musoke virus infection and Marburg Ravn virus infection comprising a chimeric GP protein according to claim 10.

42. A vaccine against Ebola Zaire virus infection and Marburg Musoke virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 25.

43. A vaccine against Ebola Zaire virus infection and Marburg Musoke virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 26.

44. A vaccine against Marburg Musoke virus infection and Marburg Ravn virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 27.

45. A vaccine against Marburg Musoke virus infection and Marburg Ravn virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 28.

46. A pharmaceutical composition comprising a chimeric peptide encoded by any of SEQ ID NO:1, 3, 5, or 7 in a pharmaceutically acceptable amount, in a pharmaceutically acceptable carrier and/or adjuvant.

47. A bivalent filovirus vaccine antigen comprising a chimeric GP protein comprising GP1 or a portion thereof from a first filovirus and GP2 or a portion thereof from a second filovirus, said antigen able to elicit an immune response to two filoviruses in a subject.

48. A multivalent filovirus vaccine antigen comprising a chimeric GP protein wherein GP1 and GP2 are comprised of portions of GP1 and GP2 chosen from different filoviruses, said antigen able to elicit an immunt response to more than two filoviruses in a subject.

```
=> e hevey m c/in
E1            2     HEVESI LASZLO/IN
E2            1     HEVESY WILLIAM K/IN
E3            0 --> HEVEY M C/IN
E4            1     HEVEY MAURICE O/IN
E5            1     HEVEY MAURICE R/IN
E6            3     HEVEY MICHAEL C/IN
E7            6     HEVEY RICHARD C/IN
E8            1     HEVEY RONALD W/IN
E9            1     HEVEY STEPHEN J/IN
E10           3     HEVEZI JAMES M/IN
E11           6     HEVEZI PETER/IN
E12           1     HEVEZI PETER A/IN

=> s e6
L2            3 "HEVEY MICHAEL C"/IN

=> s l2 not l1
L3            2 L2 NOT L1

=> d l3,ti,1-2

L3   ANSWER 1 OF 2  USPATFULL on STN
TI     Marburg virus vaccines

L3   ANSWER 2 OF 2  USPATFULL on STN
TI     Marburg virus vaccines


=> d l3,cbib,ab,clm,1-2

L3   ANSWER 1 OF 2  USPATFULL on STN
2003:219300 Marburg virus vaccines.
    Hevey, Michael C., Frederick, MD, UNITED STATES
    Negley, Diane L., Frederick, MD, UNITED STATES
    Pushko, Peter, Frederick, MD, UNITED STATES
    Smith, Jonathan F., Sabillasville, MD, UNITED STATES
```

US 2003152590 A1 20030814
APPLICATION: US 2002-267322 A1 20021009 (10)
PRIORITY: US 1998-91403P 19980629 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Using the MBGV GP, NP, and virion proteins, a method and composition for use in inducing an immune response which is protective against infection with MBGV in nonhuman primates is described.

CLM What is claimed is:

1. A recombinant DNA construct comprising: (i) a vector, and (ii) at least one of the MBGV virus DNA fragments encoding any one of GP, NP, VP40, VP35, VP30, VP24, and GPΔTM.

2. A recombinant DNA construct according to claim 1 wherein said vector is an expression vector.

3. A recombinant DNA construct according to claim 1 wherein said vector is a prokaryotic vector.

4. A recombinant DNA construct according to claim 1 wherein said vector is a eukaryotic vector.

5. The recombinant DNA construct of claim 1 wherein said vector is a VEE virus replicon vector.

6. The recombinant DNA construct according to claim 5 wherein said MBGV virus proteins are from strain Musoke.

7. The recombinant DNA construct according to claim 5 wherein said construct is pRep Mus GP.

8. The recombinant DNA construct according to claim 5 wherein said construct is pRep Mus NP.

9. The recombinant DNA construct according to claim 5 wherein said construct is pRep Mus VP40.

10. The recombinant DNA construct according to claim 5 wherein said construct is pRep Mus VP35.

11. The recombinant DNA construct according to claim 5 wherein said construct is pRep Mus VP30.

12. The recombinant DNA construct according to claim 5 wherein said construct is pRep Mus VP24.

13. The recombinant DNA construct according to claim 5 wherein said construct is pRep Mus GPΔTM.

14. Self replicating RNA produced from the construct of any of claim 7, 8, 9, 10, 11, 12, or 13.

15. Infectious alphavirus particles produced from packaging the self replicating RNA of claim 14.

16. A pharmaceutical composition comprising infectious alphavirus particles according to claim 15 in an effective immunogenic amount in a pharmaceutically acceptable carrier and/or adjuvant.

17. A host cell transformed with a recombinant DNA construct according to claim 5.

18. A host cell according to claim 17 wherein said host cell is prokaryotic.

19. A host cell according to claim 17 wherein said host cell is eukaryotic.

20. A method for producing MBGV virus proteins comprising culturing the cells according to claim 18 under conditions such that said DNA fragment is expressed and said MBGV protein is produced.

21. A method for producing MBGV proteins comprising culturing the cells according to claim 19 under conditions such that said DNA fragment is expressed and said MBGV protein is produced.

22. A vaccine for MBGV comprising viral particles containing one or more replicon RNA encoding one or more MBGV proteins selected from the group consisting of GP, NP, VP24, VP30, VP35, VP40, and GPΔTM.

23. A pharmaceutical composition comprising the self replication RNA of

acceptable carrier and/or adjuvant.

24. A pharmaceutical composition comprising one or more recombinant DNA constructs chosen from the group consisting of pRep Mus GP, pRep Mus GPΔTM, pRep Mus NP, pRep Mus VP40, pRep Mus VP35, pRep Mus VP30, pRep Mus VP24 in a pharmaceutically acceptable amount, in a pharmaceutically accpetable carrier/and or adjuvant.

L3 ANSWER 2 OF 2 USPATFULL on STN
2003:40417 Marburg virus vaccines.
Hevey, Michael C., Frederick, MD, United States
Negley, Diane L., Frederick, MD, United States
Pushko, Peter, Frederick, MD, United States
Smith, Jonathan F., Sabillasville, MD, United States
Schmaljohn, Alan L., Frederick, MD, United States
The United States of America as represented by the Secretary of the Army, Washington, DC, United States (U.S. government)
US 6517842 B1 20030211
APPLICATION: US 1999-336910 19990621 (9)
PRIORITY: US 1998-91403P 19980629 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention here relates to recombinant DNA constructs which comprise a Venezuelan equine encephalitis replicon vector and at least one DNA fragment encoding a protective antigen from the Marburg virus. The DNA constructs are useful for inducing an immune response which is protective against infection with Marburg virus in nonhuman primates.
CLM What is claimed is:
1. A recombinant DNA construct comprising: (i) a Venezuelan equine encephalitis replicon vector, and (ii) at least one DNA fragment encoding a protective antigen from the Musoke strain of the Marburg virus.

2. The recombinant DNA construct according to claim 1 wherein said construct is pRep Mus GP.

3. The recombinant DNA construct according to claim 1 wherein said construct is pRep Mus NP.

4. The recombinant DNA construct according to claim 1 wherein said construct is pRep Mus VP40.

5. The recombinant DNA construct according to claim 1 wherein said construct is pRep Mus VP35.

6. The recombinant DNA construct according to claim 1 wherein said construct is pRep Mus VP30.

7. The recombinant DNA construct according to claim 1 wherein said construct is pRep Mus VP24.

8. The recombinant DNA construct according to claim 1 wherein said construct is pRep Mus GPΔTM.

9. A host cell transformed with a recombinant DNA construct according to claim 1.

10. A host cell according to claim 9 wherein said host cell is prokaryotic.

11. A host cell according to claim 9 wherein said host cell is eukaryotic.

12. A pharmaceutical composition comprising one or more recombinant DNA constructs chosen from the group consisting of pRep Mus GP, pRep Mus GPΔTM, pRep Mus NP, pRep Mus VP40, pRep Mus VP35, pRep Mus VP30, pRep Mus VP24 in a pharmaceutically acceptable amount, in a pharmaceutically accpetable carrier/and or adjuvant.

```
=> e schmaljohn a l/in
E1          27      SCHMALIX CHARLES KENNETH/IN
E2           1      SCHMALIX WOLFGANG/IN
E3           0 -->  SCHMALJOHN A L/IN
E4           1      SCHMALJOHN ALAN/IN
E5          11      SCHMALJOHN ALAN L/IN
E6          12      SCHMALJOHN CONNIE S/IN
E7           1      SCHMALL DAVID/IN
E8           2      SCHMALL KARL H/IN
```

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E10           1     SCHMALL MARKUS/IN
E11           3     SCHMALL ROBERT A/IN
E12           2     SCHMALLEGGER HELMUT/IN

=> s e4-e5
              1 "SCHMALJOHN ALAN"/IN
             11 "SCHMALJOHN ALAN L"/IN
L4           12 ("SCHMALJOHN ALAN"/IN OR "SCHMALJOHN ALAN L"/IN)

=> s l4 and (filovir? or marburg or ebola)
           1055 FILOVIR?
           1371 MARBURG
           1336 EBOLA
L5            9 L4 AND (FILOVIR? OR MARBURG OR EBOLA)

=> s l5 not l1
L6            8 L5 NOT L1

=> s l6 not l2
L7            6 L6 NOT L2

=> d l7,ti,1-6

L7   ANSWER 1 OF 6  USPATFULL on STN
TI     Generation of virus-like particles and use as panfilovirus vaccine

L7   ANSWER 2 OF 6  USPATFULL on STN
TI     Ebola virion proteins expressed from venezuelan equine encephalitis
       (VEE) virus replicons

L7   ANSWER 3 OF 6  USPATFULL on STN
TI     Generation of virus-like particles and demonstration of lipid rafts as
       sites of filovirus entry and budding

L7   ANSWER 4 OF 6  USPATFULL on STN
TI     Monoclonal antibodies to Ebola glycoprotein

L7   ANSWER 5 OF 6  USPATFULL on STN
TI     EBOLA VIRION PROTEINS EXPRESSED FROM VENEZUELAN EQUINE ENCEPHALITIS
       (VEE) VIRUS REPLICONS

L7   ANSWER 6 OF 6  USPATFULL on STN
TI     Genetic induction of anti-viral immune response and genetic vaccine for
       filovirus


=> d l7,cbib,ab,clm,1-6

L7   ANSWER 1 OF 6  USPATFULL on STN
2005:305386 Generation of virus-like particles and use as panfilovirus vaccine.
    Bavari, Sina, Frederick, MD, UNITED STATES
    Aman, M. Javad, Gaithersburg, MD, UNITED STATES
    Schmaljohn, Alan L., Millers, MD, UNITED STATES
    Warfield, Kelly L., Frederick, MD, UNITED STATES
    Swenson, Dana, Frederick, MD, UNITED STATES
    US 2005266023 A1 20051201
    APPLICATION: US 2005-105031  A1  20050413 (11)
    PRIORITY: US 2001-338936P  20011107 (60)
    US 2004-562800P  20040413 (60)
    US 2004-562801P  20040413 (60)
    DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     In this application are described filovirus-like particles for both
       Ebola and Marburg and their use as a diagnostic and therapeutic
       agent as well as a filovirus vaccine. Also described is the
       association of Ebola and Marburg with lipid rafts during assembly
       and budding, and the requirement of functional rafts for entry of
       filoviruses into cells.
CLM    What is claimed is:
       1. A filovirus virus like particle, VLP, comprising filovirus
       envelope glycoprotein, GP, and filovirus matrix protein, VP40.

       2. A filovirus VLP, produced by expressing in a cell a polynucleotide
       encoding filovirus envelope glycoprotein, GP, and filovirus matrix
       protein, VP40 such that said polynucleotide is expressed and said VLP is
       produced.

       3. A VLP of claim 1 where said filovirus is chosen from the group
       consisting of Ebola and Marburg.

       4. A VLP of claim 2 where said filovirus is chosen from the group
       consisting of Ebola and Marburg.
```

5. A method for inhibiting the association of a **filovirus** envelope glycoprotein GP with lipid rafts, comprising inhibiting palmitoylation at cysteine residues 670 and 672 of said GP.

6. A method for preventing **filovirus** trafficking into and out of a cell comprising disrupting lipid rafts of said cell.

7. The method of claim 5 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

8. The method of claim 6 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

9. The method according to claim 6 wherein said rafts are disrupted with a cholesterol destabilizing agent.

10. The method according to claim 8 wherein said agents are filipin and nystatin.

11. A method for preventing **filovirus** trafficking said method comprising introducing to a cell cholesterol synthesis inhibitors.

12. The method of claim 11 wherein said cholesterol synthesis inhibitor is methyl-β-cyclodextrin.

13. A **filovirus** vaccine comprising VLP according to claim 1.

14. A **filovirus** vaccine comprising VLP according to claim 2.

15. A **filovirus** vaccine according to claim 14 further comprising an adjuvant.

16. The vaccine of claim 15 wherein said adjuvant is chosen from the group consisting of: RIB1, QS21 and LT(R192G).

17. A **filovirus** vaccine according to claim 13 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

18. A **filovirus** vaccine according to claim 14 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

19. A **filovirus** vaccine comprising VLP according to claim 1 and a nucleic acid encoding an agent capable of eliciting an immune response against said **filovirus**.

20. A method for introducing an agent into a cell, comprising packaging said agent into a of claim 1, producing a packed VLP and allowing the packed VLP to enter said cell.

21. The method according to claim 20 wherein said VLP is a **filovirus** virus like particle, comprising **filovirus** envelope glycoprotein, GP, and **filovirus** matrix protein, VP40.

22. The method according to claim 21 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

23. The method according to claim 20 wherein said VLP is produced by expressing in a cell a polynucleotide encoding **filovirus** envelope glycoprotein, GP, and **filovirus** matrix protein, VP40 such that said polynucleotide is expressed and said VLP is produced.

24. The method according to claim 23 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

25. An **Ebola** VLP-producing cell comprising a mammalian cell expressing **Ebola** GP and VP40.

26. A method for testing an agent involved in **filovirus** budding, comprising introducing said agent to a cultured cell according to claim 25, producing **filovirus** VLP and monitoring the presence or absence of a change in the budding of VLP as compared to a control by measuring VLPs in supernatant of said cultured cell, wherein a reduction or increase in the number of VLP in the superntant indicates a negative or positive agent, respectively, on **filovirus** budding.

27. The method according to claim 26 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

28. A method for inhibiting **Ebola** virus infection in a cell comprising administering to said cell lipid raft-disrupting agents.

29. The method according to claim 28 wherein said agents are Filipin and

30. A method for detecting **Ebola** virus infection comprising contacting a sample from a subject suspected of having **Ebola** virus infection with an **Ebola** VLP according to claim 3 and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Ebola** VLP and antibodies specific therefor in said sample.

31. A kit for the detection of **Ebola** virus infection comprising **Ebola** VLPs according to claim 3.

32. A method for detecting **Marburg** virus infection comprising contacting a sample from a subject suspected of having **Marburg** virus infection with a **Marburg** VLP according to claim 3 and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Marburg** VLP and antibodies specific therefor in said sample.

33. A kit for the detection of **Marburg** virus infection comprising **Marburg** VLPs according to claim 3.

34. A kit for testing agents involved in **Ebola** budding said kit comprising a cell producing **Ebola** VLPs according to claim 25 and ancillary reagents for detecting VLPs in the supernatant of said cells when cells are cultured.

35. A **Marburg** VLP-producing cell comprising a mammalian cell expressing **Marburg** GP and VP40.

36. A kit for testing agents involved in **Marburg** budding said kit comprising a cell producing **Marburg** VLPs according to claim 35 and ancillary reagents for detecting VLPs in the supernatant of said cells when cells are cultured.

37. An immunogenic composition comprising, in a physiologically acceptable vehicle, **Ebola** VLPs according to claim 4.

38. The immunogenic composition according to claim 37, which induces an **Ebola** specific immune response in a subject.

39. The immunogenic composition according to claim 37 which further comprises an adjuvant to enhance the immune response.

40. The immunogenic composition of claim 37, wherein said **Ebola** VLPs are produced by expressing in a mammalian cell **Ebola** GP and **Ebola** VP40.

41. A method for stimulating an **Ebola** virus specific immune response, said method comprising administering to a subject an immunologically sufficient amount of **Ebola** VLPs according to claim 4 in a physiologically acceptable vehicle.

42. An immunogenic composition comprising, in a physiologically acceptable vehicle, **Marburg** VLPs according to claim 4.

43. The immunogenic composition according to claim 42, which induces a **Marburg** specific immune response in a subject.

44. The immunogenic composition according to claim 42 which further comprises an adjuvant to enhance the immune response.

45. The immunogenic composition of claim 42, wherein said **Marburg** VLPs are produced by expressing in a mammalian cell **Marburg** GP and **Marburg** VP40.

46. A method for stimulating a **Marburg** virus specific immune response, said method comprising administering to a subject an immunologically sufficient amount of **Marburg** VLPs according to claim 4 in a physiologically acceptable vehicle.

47. A panfilovirus vaccine comprising a mixture of EBOV and MARV VLPs according to claim 4.

48. A MARV vaccine protective against infection with MARV-Musoke, MARV-Ravn, and MARV-Ci67, comprising MARV VLPs according to claim 4 consisting essentially of GP and VP40 from MARV-Musoke.

L7 ANSWER 2 OF 6 USPATFULL on STN

2004:190090 **Ebola** virion proteins expressed from venezuelan equine encephalitis (VEE) virus replicons.

Hart, Mary K., Frederick, MD, UNITED STATES
Wilson, Julie A., Frederick, MD, UNITED STATES

Smith, Jonathan F., Sabillasville, MD, UNITED STATES
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US 2004146859 A1 20040729
APPLICATION: US 2003-696633 A1 20031029 (10)
PRIORITY: US 1998-91403P 19980629 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Using the **Ebola** GP, NP, VP24, VP30, VP35 and VP40 virion proteins, a method and composition for use in inducing an immune response which is protective against infection with **Ebola** virus is described.

CLM What is claimed is:

1. A DNA fragment which encodes a GP **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:1, or a polynucleotide fragment comprising at least 15 nucleotides.

2. A DNA fragment which encodes a NP **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:2, or a polynucleotide fragment comprising at least 15 nucleotides.

3. A DNA fragment which encodes a VP24 **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:3, or a polynucleotide fragment comprising at least 15 nucleotides.

4. A DNA fragment which encodes a VP30 **Ebola** protein, said DNA fragment comprising the sequence specified in any of SEQ ID NO:4 and SEQ ID NO:7, or a polynucleotide fragment comprising at least 15 nucleotides.

5. A DNA fragment which encodes a VP35 **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:5, or a polynucleotide fragment comprising at least 15 nucleotides.

6. A DNA fragment which encodes a VP40 **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:6, or a polynucleotide fragment comprising at least 15 nucleotides.

7. A DNA fragment which encodes a GP **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:17 or a conservative substitution thereof.

8. A DNA fragment which encodes a NP **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:18 or a conservative substitution thereof.

9. A DNA fragment which encodes a VP24 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:19 or a conservative substitution thereof.

10. A DNA fragment which encodes a VP30 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in any of SEQ ID NO:20 and SEQ ID NO:23 or a conservative substitution thereof.

11. A DNA fragment which encodes a VP35 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:21 or a conservative substitution thereof.

12. A DNA fragment which encodes a VP40 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:22 or a conservative substitution thereof.

13. A recombinant DNA construct comprising: (i) a vector, and (ii) at least one of the **Ebola** virus DNA fragments chosen from the group consisting of SEQ ID NO:1, 2, 3, 4, 5, 6 and 7 or a fragment thereof comprising at least 15 nucleotides.

14. A recombinant DNA construct comprising: (i) a vector, and (ii) at least one of the **Ebola** virus DNA fragments chosen from the group consisting of SEQ ID NO: 17, 18, 19, 20, 21, 22, 23, 24 and 25 or a conservative substitution thereof.

15. The recombinant DNA construct of claim 13 wherein said DNA fragment induces a cytotoxic T lymphocyte, response or antibody response.

16. The recombinant DNA construct of claim 14 wherein said DNA fragment induces a cytotoxic T lymphocyte response or antibody response.

17. A recombinant DNA construct according to claim 13 wherein said vector is an expression vector.

18. A recombinant DNA construct according to claim 13 wherein said vector is a prokaryotic vector.

19. A recombinant DNA construct according to claim 13 wherein said vector is a eukaryotic vector.

20. A recombinant DNA construct according to claim 14 wherein said vector is an expression vector.

21. A recombinant DNA construct according to claim 14 wherein said vector is a prokaryotic vector.

22. A recombinant DNA construct according to claim 14 wherein said vector is a eukaryotic vector.

23. The recombinant DNA construct of claim 17 wherein said vector is a VEE virus replicon vector.

24. The recombinant DNA construct of claim 20 wherein said vector is a VEE virus replicon vector.

25. The recombinant DNA construct according to claim 23 wherein said **Ebola** virus DNA fragments are from **Ebola** Zaire 1976.

26. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP24.

27. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP30.

28. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP35.

29. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP40.

30. The recombinant DNA construct according to claim 25 wherein said construct is for VRepEboNP.

31. The recombinant DNA construct according to claim 25 wherein said construct is for VRepEboGP.

32. The recombinant DNA construct according to claim 25 wherein said construct is for VRepEboVP30(#2).

33. Self replicating RNA produced from a construct chosen from the group consisting of EboVP24ReP, EboVP30ReP, EboVP35ReP, EboVP40ReP, EboVPNPReP, EboVPGPReP, and EboVP30ReP(#2).

34. Infectious alphavirus particles produced from packaging the self replicating RNA of claim 33.

35. A pharmaceutical composition comprising infectious alphavirus particles according to claim 34 in an effective immunogenic amount in a pharmaceutically acceptable carrier and/or adjuvant.

36. A host cell transformed with a recombinant DNA construct-according to claim 13.

37. A host cell transformed with a recombinant DNA construct according to claim 14.

38. A host cell according to claim 36 wherein said host cell is prokaryotic.

39. A host cell according to claim 36 wherein said host cell is eukaryotic.

40. A host cell according to claim 37 wherein said host cell is prokaryotic.

41. A host cell according to claim 37 wherein said host cell is eukaryotic.

42. A method for producing **Ebola** virus proteins comprising culturing the cells according to claim 36 under conditions such that said DNA fragment is expressed and said **Ebola** protein is produced.

43. A method for producing **Ebola** virus proteins comprising culturing the cells according to claim 37 under conditions such that said DNA fragment is expressed and said **Ebola** protein is produced.

44. A method for producing **Ebola** virus proteins comprising culturing the cells according to claim 38 under conditions such that said DNA fragment is expressed and said **Ebola** protein is produced.

45. A method for producing **Ebola** virus proteins comprising culturing the cells according to claim 39 under conditions such that said DNA fragment is expressed and said **Ebola** protein is produced.

46. An isolated and purified **Ebola** GP protein specified in SEQ ID NO:17 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

47. An isolated and purified **Ebola** NP protein specified in SEQ ID NO:18 and conservative substitutions thereof or an immunologically identifiable portion thereof.

48. An isolated and purified **Ebola** VP24 protein specified in SEQ ID NO:19 and conservative substitutions thereof or an immunologically identifiable portion thereof.

49. An isolated and purified **Ebola** VP30 protein specified in any of SEQ ID NO:20 and SEQ ID NO:23 and conservative substitutions thereof or an immunologically identifiable portion thereof.

50. An isolated and purified **Ebola** VP35 protein specified in SEQ ID NO:21 and conservative substitutions thereof or an immunologically identifiable portion thereof.

51. An isolated and purified **Ebola** VP40 protein specified in SEQ ID NO:22 and conservative substitutions thereof or an immunologically identifiable portion thereof.

52. An antibody to a peptide encoded by the sequence specified in SEQ ID NO:17, 18, 19, 20, 21, 22, 23, 24, and 25.

53. A method for detecting **Ebola** virus infection comprising contacting a sample from a subject suspected of having **Ebola** virus infection with a antibody according to claim 52 and detecting the presence or absence by detecting the presence or absence of a complex formed between the **Ebola** protein and antibodies specific therefor.

54. A method for detecting the presence or absence of **Ebola** virus GP RNA in a sample using the polymerase chain reaction using primers for **Ebola** GP nucleic acid sequence specified in SEQ ID NO:1 for GP.

55. An **Ebola** infection diagnostic kit comprising at least 12 consecutive nucleotides of SEQ ID NO:1 specific for the amplification of DNA or RNA of **Ebola** virus in a sample using the polymerase chain reaction and ancillary reagents suitable for use in such a reaction for detecting the presence or absence of **Ebola** virus DNA or RNA in a sample.

56. A vaccine for **Ebola** comprising alphavirus particles of claim 34.

57. A method for the diagnosis of **Ebola** virus infection comprising the steps of: (i) contacting a sample from an individual suspected of having **Ebola** virus infection with an antibody to **Ebola** proteins according to claim 52; and (ii) detecting the presence or absence of **Ebola** virus infection by detecting the presence or absence of a complex formed between **Ebola** proteins and antibodies specific therefor.

58. A pharmaceutical composition comprising the self replicating RNA of claim 33 in an effective immunogenic amount in a pharmaceutically acceptable carrier and/or adjuvant.

59. A pharmaceutical composition comprising one or more recombinant DNA constructs chosen from the group consisting of VRepEboVP24, VRepEboVP30, VRepEboVP35, VRepEboVP40, VRepEboNP, VRepEboGP, and VRepEboVP30(#2), in a pharmaceutically acceptable amount, in a pharmaceutically accpetable carrier and/or adjuvant.

60. A pharmaceutical composition comprising comprising a peptide encoded by any of SEQ ID NO:24 and SEQ ID NO:25, in a pharmaceutically acceptable amount, in a pharmaceutically acceptable carrier and/or adjuvant.

L7 ANSWER 3 OF 6 USPATFULL on STN
2004:76190 Generation of virus-like particles and demonstration of lipid rafts as sites of **filovirus** entry and budding.
Bavari, Sina, Frederick, MD, UNITED STATES
Aman, M. Javad, Potomac, MD, UNITED STATES
Schmaljohn, Alan L., Frederick, MD, UNITED STATES
US 2004057967 A1 20040325
APPLICATION: US 2002-289839 A1 20021107 (10)
PRIORITY: US 2001-338936P 20011107 (60)
DOCUMENT TYPE: Utility; APPLICATION.

AB In this application is described a method for the formation of **filovirus**-like particles for both **Ebola** and **Marburg** and their use as a diagnostic and therapeutic agent as well as a **filovirus** vaccine. Also described is the association of **Ebola** and **Marburg** with lipid rafts during assembly and budding, and the requirement of functional rafts for entry of **filoviruses** into cells.

CLM What is claimed is:

1. A **filovirus** virus like particle, VLP, comprising **filovirus** envelope glycoprotein, GP, and **filovirus** matrix protein, VP40.

2. A **filovirus** VLP, produced by expressing in a cell a polynucleotide encoding **filovirus** envelope glycoprotein, GP, and **filovirus** matrix protein, VP40 such that said polynucleotide is expressed and said VLP is produced.

3. A VLP of claim 1 where said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

4. A VLP of claim 2 where said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

5. A method for inhibiting the association of a **filovirus** envelope glycoprotein GP with lipid rafts, comprising inhibiting palmitoylation at cysteine residues 670 and 672 of said GP.

6. A method for preventing **filovirus** trafficking into and out of a cell comprising disrupting lipid rafts of said cell.

7. The method of claim 5 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

8. The method of claim 6 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

9. The method according to claim 6 wherein said rafts are disrupted with a cholesterol destabilizing agent.

10. The method according to claim 8 wherein said agents are filipin and nystatin.

11. A method for preventing **filovirus** trafficking said method comprising introducing to a cell cholesterol synthesis inhibitors.

12. The method of claim 11 wherein said cholesterol synthesis inhibitor is methyl-β-cyclodextrin.

13. A **filovirus** vaccine comprising VLP according to claim 1.

14. A **filovirus** vaccine comprising VLP according to claim 2.

15. A **filovirus** vaccine according to claim 13 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

16. A **filovirus** vaccine according to claim 14 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

17. A **filovirus** vaccine comprising VLP and a nucleic acid encoding an agent capable of eliciting an immune response against said **filovirus**.

18. A method for introducing an agent into a cell, comprising packaging said agent into a VLP producing a packed VLP and allowing the packed VLP to enter said cell.

19. The method according to claim 18 wherein said VLP is that of claim 1.

20. The method according to claim 19 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

21. The method according to claim 18 wherein said VLP is that of claim 2.

22. The method according to claim 21 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

23. A method for testing an agent involved in **filovirus** budding, comprising introducing said agent to a cultured cell producing **filovirus** VLP and monitoring the presence or absence of a change in the budding of VLP as compared to a control by measuring VLPs in supernatant of said cultured cell, wherein a reduction or increase in the number of VLP in the superntant indicates a negative or positive agent, respectively, on **filovirus** budding.

24. The method according to claim 23 wherein said **filovirus** is chosen from the group consisting of **Ebola** and **Marburg**.

25. A method for inhibiting **Ebola** virus infection in a cell comprising administering to said cell lipid raft-disrupting agents.

26. The method according to claim 25 wherein said agents are Filipin and Nystatin.

27. A method for detecting **Ebola** virus infection comprising contacting a sample from a subject suspected of having **Ebola** virus infection with an **Ebola** VLP according to claim 3 and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Ebola** VLP and antibodies specific therefor in said sample.

28. A kit for the detection of **Ebola** virus infection comprising **Ebola** VLPs according to claim 3.

29. A method for detecting **Marburg** virus infection comprising contacting a sample from a subject suspected of having **Marburg** virus infection with a **Marburg** VLP according to claim 3 and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Marburg** VLP and antibodies specific therefor in said sample.

30. A kit for the detection of **Marburg** virus infection comprising **Marburg** VLPs according to claim 3.

31. A kit for testing agents involved in **Ebola** budding said kit comprising a cell producing **Ebola** VLPs and ancillary reagents for detecting VLPs in the supernatant of said cells when cells are cultured.

32. An **Ebola** VLP-producing cell comprising a mammalian cell expressing **Ebola** GP and VP40.

33. A kit for testing agents involved in **Marburg** budding said kit comprising a cell producing **Marburg** VLPs and ancillary reagents for detecting VLPs in the supernatant of said cells when cells are cultured.

34. A **Marburg** VLP-producing cell comprising a mammalian cell expressing **Marburg** GP and VP40.

35. An immunogenic composition comprising, in a physiologically acceptable vehicle, **Ebola** VLPs.

36. The immunogenic composition according to claim 35, which induces an **Ebola** specific immune response in a subject.

37. The immunogenic composition according to claim 35 which further comprises an adjuvant to enhance the immune response.

38. The immunogenic composition of claim 35, wherein said **Ebola** VLPs are produced by expressing in a mammalian cell **Ebola** GP and **Ebola** VP40.

39. A method for stimulating an **Ebola** virus specific immune response, said method comprising administering to a subject an immunologically sufficient amount of **Ebola** VLPs in a physiologically acceptable vehicle.

40. An immunogenic composition comprising, in a physiologically acceptable vehicle, **Marburg** VLPs.

41. The immunogenic composition according to claim 40, which induces a **Marburg** specific immune response in a subject.

42. The immunogenic composition according to claim 40 which further comprises an adjuvant to enhance the immune response.

43. The immunogenic composition of claim 40, wherein said **Marburg** VLPs are produced by expressing in a mammalian cell **Marburg** GP and **Marburg** VP40.

44. A method for stimulating a **Marburg** virus specific immune response, said method comprising administering to a subject an immunologically sufficient amount of **Marburg** VLPs in a physiologically acceptable vehicle.

L7 ANSWER 4 OF 6 USPATFULL on STN
2003:268051 Monoclonal antibodies to **Ebola** glycoprotein.
Hart, Mary K., Frederick, MD, United States
Wilson, Julie A., Frederick, MD, United States

The United States of America as represented by the Secretary of the Army, Washington, DC, United States (U.S. government)
US 6630144 B1 20031007
APPLICATION: US 2000-650086 20000829 (9)
PRIORITY: US 1999-151505P 19990830 (60)
DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In this application are described **Ebola** GP monoclonal antibodies and epitopes recognized by these monoclonal antibodies. Also provided are mixtures of antibodies of the present invention, as well as methods of using individual antibodies or mixtures thereof for the detection, prevention, and/or therapeutical treatment of **Ebola** virus infections in vitro and in vivo.

CLM What is claimed is:

1. An isolated monoclonal antibody which recognizes **Ebola** virus GP, wherein the epitope that binds or is recognized by said antibody is within SEQ ID NO:6 or SEQ ID NO:8.

2. The antibody according to claim 1, wherein the antibody binds **Ebola** virus in vitro.

3. The antibody according to claim 1, wherein the antibody immunoprecipitates GP from supernatants or cell lysates of cell cultures infected with **Ebola** virus.

4. The antibody according to claim 1 wherein said epitope is within SEQ ID NO:6, and is further within SEQ ID NO:7.

5. The antibody according to claim 1 wherein said epitope is within SEQ ID NO:8, and is further within SEQ ID NO:9.

6. The antibody according to claim 1, wherein said antibody is produced by hybridoma cell line EGP 13F6-1-2 with Accession no. PTA-373.

7. An antibody which competes with the antibody of claim 6 for binding to **Ebola** virus GP.

8. The antibody according to claim 1, wherein said antibody is produced by hybridoma cell line EGP 6D3-1-1 with Accession no. PTA-374.

9. An antibody which competes with the antibody of claim 8 for binding to **Ebola** virus GP.

10. The antibody according to claim 1, wherein said antibody is produced by hybridoma cell line EGP 13C6-1-1 with Accession no. PTA-375.

11. An antibody which competes with the antibody of claim 10 for binding to **Ebola** virus GP.

12. The antibody according to claim 1, wherein said antibody is produced by hybridoma cell line EGP 6D8-1-2 with Accession no. PTA-376.

13. An antibody which competes with the antibody of claim 12 for binding to **Ebola** virus GP.

14. The antibody according to claim 1, wherein said antibody is produced by hybridoma cell line EGP 12B5-1-1 with Accession no. PTA-436.

15. An antibody which competes with the antibody of claim 14 for binding to **Ebola** virus GP.

16. A mixture comprising **Ebola** virus antibodies comprising one or more antibodies selected from the group consisting of an antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373; an antibody produced by hybridoma EGP 6D3-1-1 accession no. PTA 374; an antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; an antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376; and an antibody produced by hybridoma EGP 12B5-1-1 accession no. PTA 436.

17. A monoclonal antibody producing cell line that produces a monoclonal antibody according to claim 1.

18. The cell line according to claim 17, selected from the group consisting of cell line EGP 13F6-1-2 (ATCC accession no. PTA 373), cell line EGP 6D3-1-1 (ATCC accession no. PTA 374), cell line EGP 13C6-1-1 (ATCC accession no. PTA 375), cell line EGP 6D8-1-2 (ATCC accession no. PTA 376), and cell line EGP 12B5-1-1 (ATCC accession no. PTA 436).

19. An antiidiotypic antibody produced from any of the monoclonal antibodies selected from the group consisting of MAb13F6, MAb 6D3, MAb 13C6, MAb 6D8, and MAb 12B5.

for binding to GP with an antibody selected from the group consisting of MAb13F6, MAb 6D3, MAb 13C6, MAb 6D8, and MAb 12B5.

L7 ANSWER 5 OF 6 USPATFULL on STN

2002:294539 **EBOLA** VIRION PROTEINS EXPRESSED FROM VENEZUELAN EQUINE ENCEPHALITIS (VEE) VIRUS REPLICONS.

HART, MARY K., FREDERICK, MD, UNITED STATES
WILSON, JULIE A., FREDERICK, MD, UNITED STATES
PUSHKO, PETER, FREDERICK, MD, UNITED STATES
SMITH, JONATHAN F., SABILLASVILLE, MD, UNITED STATES
SCHMALJOHN, ALAN L., FREDERICK, MD, UNITED STATES
US 2002164582 A1 20021107
APPLICATION: US 1999-337946 A1 19990622 (9)
PRIORITY: US 1998-91403P 19980629 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Using the **Ebola** GP, NP, VP24, VP30, VP35 and VP40 virion proteins, a method and composition for use in inducing an immune response which is protective against infection with **Ebola** virus is described.

CLM What is claimed is:

1. A DNA fragment which encodes a GP **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:1, or a polynucleotide fragment comprising at least 15 nucleotides.

2. A DNA fragment which encodes a NP **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:2, or a polynucleotide fragment comprising at least 15 nucleotides.

3. A DNA fragment which encodes a VP24 **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:3, or a polynucleotide fragment comprising at least 15 nucleotides.

4. A DNA fragment which encodes a VP30 **Ebola** protein, said DNA fragment comprising the sequence specified in any of SEQ ID NO:4 and SEQ ID NO:7, or a polynucleotide fragment comprising at least 15 nucleotides.

5. A DNA fragment which encodes a VP35 **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:5, or a polynucleotide fragment comprising at least 15 nucleotides.

6. A DNA fragment which encodes a VP40 **Ebola** protein, said DNA fragment comprising the sequence specified in SEQ ID NO:6, or a polynucleotide fragment comprising at least 15 nucleotides.

7. A DNA fragment which encodes a GP **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:17 or a conservative substitution thereof.

8. A DNA fragment which encodes a NP **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:18 or a conservative substitution thereof.

9. A DNA fragment which encodes a VP24 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:19 or a conservative substitution thereof.

10. A DNA fragment which encodes a VP30 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in any of SEQ ID NO:20 and SEQ ID NO:23 or a conservative substitution thereof.

11. A DNA fragment which encodes a VP35 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:21 or a conservative substitution thereof.

12. A DNA fragment which encodes a VP40 **Ebola** protein said DNA fragment comprising a DNA sequence encoding at least 5 amino acids specified in SEQ ID NO:22 or a conservative substitution thereof.

13. A recombinant DNA construct comprising: (i) a vector, and (ii) at least one of the **Ebola** virus DNA fragments chosen from the group consisting of SEQ ID NO:1, 2, 3, 4, 5, 6 and 7 or a fragment thereof comprising at least 15 nucleotides.

14. A recombinant DNA construct comprising: (i) a vector, and (ii) at least one of the **Ebola** virus DNA fragments chosen from the group consisting of SEQ ID NO: 17, 18, 19, 20, 21, 22, 23, 24 and 25 or a conservative substitution thereof.

15. The recombinant DNA construct of claim 13 wherein said DNA fragment

16. The recombinant DNA construct of claim 14 wherein said DNA fragment induces a cytotoxic T lymphocyte response or antibody response.

17. A recombinant DNA construct according to claim 13 wherein said vector is an expression vector.

18. A recombinant DNA construct according to claim 13 wherein said vector is a prokaryotic vector.

19. A recombinant DNA construct according to claim 13 wherein said vector is a eukaryotic vector.

20. A recombinant DNA construct according to claim 14 wherein said vector is an expression vector.

21. A recombinant DNA construct according to claim 14 wherein said vector is a prokaryotic vector.

22. A recombinant DNA construct according to claim 14 wherein said vector is a eukaryotic vector.

23. The recombinant DNA construct of claim 17 wherein said vector is a VEE virus replicon vector.

24. The recombinant DNA construct of claim 20 wherein said vector is a VEE virus replicon vector.

25. The recombinant DNA construct according to claim 23 wherein said **Ebola** virus DNA fragments are from **Ebola** Zaire 1976.

26. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP24.

27. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP30.

28. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP35.

29. The recombinant DNA construct according to claim 25 wherein said construct is VRepEboVP40.

30. The recombinant DNA construct according to claim 25 wherein said construct is for VRepEboNP.

31. The recombinant DNA construct according to claim 25 wherein said construct is for VRepEboGP.

32. The recombinant DNA construct according to claim 25 wherein said construct is for VRepEboVP30(#2).

33. Self replicating RNA produced from a construct chosen from the group consisting of EboVP24ReP, EboVP30ReP, EboVP35ReP, EboVP40ReP, EboVPNPReP, EboVPGPReP, and EboVP30ReP(#2).

34. Infectious alphavirus particles produced from packaging the self replicating RNA of claim 33.

35. A pharmaceutical composition comprising infectious alphavirus particles according to claim 34 in an effective immunogenic amount in a pharmaceutically acceptable carrier and/or adjuvant.

36. A host cell transformed with a recombinant DNA construct according to claim 13.

37. A host cell transformed with a recombinant DNA construct according to claim 14.

38. A host cell according to claim 36 wherein said host cell is prokaryotic.

39. A host cell according to claim 36 wherein said host cell is eukaryotic.

40. A host cell according to claim 37 wherein said host cell is prokaryotic.

41. A host cell according to claim 37 wherein said host cell is eukaryotic.

42. A method for producing **Ebola** virus proteins comprising culturing

fragment is expressed and said **Ebola** protein is produced.

43. A method for producing **Ebola** virus proteins comprising culturing the cells according to claim 37 under conditions such that said DNA fragment is expressed and said **Ebola** protein is produced.

44. A method for producing **Ebola** virus proteins comprising culturing the cells according to claim 38 under conditions such that said DNA fragment is expressed and said **Ebola** protein is produced.

45. A method for producing **Ebola** virus proteins comprising culturing the cells according to claim 39 under conditions such that said DNA fragment is expressed and said **Ebola** protein is produced.

46. An isolated and purified **Ebola** GP protein specified in SEQ ID NO:17 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

47. An isolated and purified **Ebola** NP protein specified in SEQ ID NO:18 and conservative substitutions thereof or an immunologically identifiable portion thereof.

48. An isolated and purified **Ebola** VP24 protein specified in SEQ ID NO:19 and conservative substitutions thereof or an immunologically identifiable portion thereof.

49. An isolated and purified **Ebola** VP30 protein specified in any of SEQ ID NO:20 and SEQ ID NO:23 and conservative substitutions thereof or an immunologically identifiable portion thereof.

50. An isolated and purified **Ebola** VP35 protein specified in SEQ ID NO:21 and conservative substitutions thereof or an immunologically identifiable portion thereof.

51. An isolated and purified **Ebola** VP40 protein specified in SEQ ID NO:22 and conservative substitutions thereof or an immunologically identifiable portion thereof.

52. An antibody to a peptide encoded by the sequence specified in SEQ ID NO:17, 18, 19, 20, 21, 22, 23, 24, and 25.

53. A method for detecting **Ebola** virus infection comprising contacting a sample from a subject suspected of having **Ebola** virus infection with a antibody according to claim 52 and detecting the presence or absence by detecting the presence or absence of a complex formed between the **Ebola** protein and antibodies specific therefor.

54. A method for detecting the presence or absence of **Ebola** virus GP RNA in a sample using the polymerase chain reaction using primers for **Ebola** GP nucleic acid sequence specified in SEQ ID NO:1 for GP.

55. An **Ebola** infection diagnostic kit comprising at least 12 consecutive nucleotides of SEQ ID NO:1 specific for the amplification of DNA or RNA of **Ebola** virus in a sample using the polymerase chain reaction and ancillary reagents suitable for use in such a reaction for detecting the presence or absence of **Ebola** virus DNA or RNA in a sample.

56. A vaccine for **Ebola** comprising alphavirus particles of claim 34.

57. A method for the diagnosis of **Ebola** virus infection comprising the steps of: (i) contacting a sample from an individual suspected of having **Ebola** virus infection with an antibody to **Ebola** proteins according to claim 52; and (ii) detecting the presence or absence of **Ebola** virus infection by detecting the presence or absence of a complex formed between **Ebola** proteins and antibodies specific therefor.

58. A pharmaceutical composition comprising the self replicating RNA of claim 33 in an effective immunogenic amount in a pharmaceutically acceptable carrier and/or adjuvant.

59. A pharmaceutical composition comprising one or more recombinant DNA constructs chosen from the group consisting of VRepEboVP24, VRepEboVP30, VRepEboVP35, VRepEboVP40, VRepEboNP, VRepEboGP, and VRepEboVP30(#2), in a pharmaceutically acceptable amount, in a pharmaceutically accpetable carrier and/or adjuvant.

60. A pharmaceutical composition comprising comprising a peptide encoded by any of SEQ ID NO:24 and SEQ ID NO:25, in a pharmaceutically acceptable amount, in a pharmaceutically acceptable carrier and/or adjuvant.

2001:36806 Genetic induction of anti-viral immune response and genetic vaccine for **filovirus**.
Haynes, Joel R., Fort Collins, CO, United States
Schmaljohn, Connie S., Frederick, MD, United States
Fuller, Deborah L., Oregon, WI, United States
Schmaljohn, Alan, Frederick, MD, United States
Jahrling, Peter B., Middletown, MD, United States
PowerJect Vaccines Inc., Madison, WI, United States (U.S. corporation)
US 6200959 B1 20010313
APPLICATION: US 1996-760615 19961204 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An approach to genetic vaccine methodology is described. A genetic construction encoding antigenic determinants of a **filovirus** is transfected into cells of the vaccinated individuals using a particle acceleration protocol so as to express the viral antigens in healthy cells to produce an immune response to those antigens.

CLM What is claimed is:
1. A method of inducing an immune response to a **Marburg** or **Ebola** virus glycoprotein in a mammal, said method comprising: (a) providing a genetic construction comprising a promoter operative in cells of the mammal and a coding region for a determinant of the glycoprotein, the genetic construction not comprising sequences necessary for replication of the virus; (b) coating copies of the genetic construction onto carrier particles small in size in relation to the size of the cells of the mammal; and (c) accelerating the coated carrier particles into epidermal cells of the mammal in vivo, thereby inducing an immune response against the glycoprotein.

2. A method as claimed in claim 1 wherein the carrier particles are accelerated by a gaseous pulse in order to accelerate the carrier particles toward the mammal.

3. A method as claimed in claim 1 wherein the protein coding region encodes a glycoprotein selected from the group consisting of **Ebola** Zaire virus gp125, **Marburg** Musoke virus gp170,and **Marburg** Ravn virus glycoprotein.

4. A method as claimed in claim 1 wherein the protein coding region comprises SEQ ID NO: 1.

5. A method as claimed in claim 1 wherein the protein coding region comprises SEQ ID NO: 3.

6. A method as claimed in claim 1 wherein the protein coding region comprises SEQ ID NO: 5.

7. A composition of matter comprising a carrier particle and a genetic construction coated onto the carrier particle, wherein the genetic construction comprises a promoter operative in the cells of a mammal and a coding region for a determinant of a **Marburg** or **Ebola** virus glycoprotein.

8. A composition as claimed in claim 7 wherein the protein coding region encodes a glycoprotein selected from the group consisting of **Ebola** Zaire virus gp125, **Marburg** Musoke virus gp170, and **Marburg** Ravn virus glycoprotein.

9. A composition as claimed in claim 7 wherein the protein coding region comprises SEQ ID NO: 1.

10. A composition as claimed in claim 7 wherein the protein coding region comprises SEQ ID NO: 3.

11. A composition as claimed in claim 7 wherein the protein coding region comprises SEQ ID No. 5.

```
=> d his

     (FILE 'HOME' ENTERED AT 10:36:34 ON 06 MAR 2006)

     FILE 'USPATFULL' ENTERED AT 10:36:47 ON 06 MAR 2006
                E GROGAN C C/IN
L1            1 S E4
                E HEVEY M C/IN
L2            3 S E6
L3            2 S L2 NOT L1
                E SCHMALJOHN A L/IN
L4           12 S E4-E5
L5            9 S L4 AND (FILOVIR? OR MARBURG OR EBOLA)
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L7           6 S L6 NOT L2

=> file wpids
COST IN U.S. DOLLARS                              SINCE FILE     TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    34.15      34.36

FILE 'WPIDS' ENTERED AT 10:39:55 ON 06 MAR 2006
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    PLEASE CHECK:
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http://www.stn-international.de/stndatabases/details/ipc_reform.html  and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

=> e grogan c c/in
E1           4     GROGAN A F/IN
E2           3     GROGAN C/IN
E3           1 --> GROGAN C C/IN
E4           3     GROGAN C W/IN
E5           6     GROGAN D/IN
E6           3     GROGAN D C/IN
E7           4     GROGAN D R/IN
E8           2     GROGAN E/IN
E9           4     GROGAN E A/IN
E10          1     GROGAN G P/IN
E11          4     GROGAN G W/IN
E12          1     GROGAN HALL M C/IN

=> s e3
L8           1 "GROGAN C C"/IN

=> d 18,bib,ab,

L8   ANSWER 1 OF 1  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN   2003-040651 [03]   WPIDS
DNC  C2003-009637
TI   New chimeric filovirus glycoprotein (GP) protein comprising GP1 and GP2,
     useful for inducing an immune response against infection of different
     filoviruses, specifically against both Ebola and Marburg viruses.
DC   B04 D16
IN   GROGAN, C C; HEVEY, M C; SCHMALJOHN, A L
PA   (GROG-I) GROGAN C C; (HEVE-I) HEVEY M C; (SCHM-I) SCHMALJOHN A L; (USSA)
     US ARMY MEDICAL RES INST INFECTIOUS DISE
CYC  84
PI   WO 2002079239   A2 20021010 (200303)* EN   94
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZM ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
            GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK
            MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US
            UZ VN YU ZW
     US 2003108560   A1 20030612 (200340)
     AU 2002303086   A1 20021015 (200432)
ADT  WO 2002079239 A2 WO 2002-US3339 20020131; US 2003108560 A1 Provisional US
     2001-267522P 20010131, US 2002-66506 20020131; AU 2002303086 A1 AU
```

FDT AU 2002303086 A1 Based on WO 2002079239
PRAI US 2001-267522P 20010131; US 2002-66506 20020131
AB WO 200279239 A UPAB: 20030113
NOVELTY - A chimeric filovirus glycoprotein (GP) protein comprising GP1 and GP2, where GP1 is from a filovirus different than that of GP2, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a DNA fragment encoding a chimeric protein above and comprising a sequence of 2252, 1841, 2046 or 2246 bp given in the specification, or their conservative substitutions;

(2) a recombinant DNA construct comprising a vector, and a DNA fragment encoding a chimeric filovirus GP protein defined above;

(3) self replicating RNA produced from the construct of (2);

(4) infectious alphavirus particles produced from packaging the self replicating RNA of (3);

(5) a pharmaceutical composition comprising infectious alphavirus particles in a pharmaceutical carrier and/or adjuvant;

(6) a host cell transformed with a recombinant DNA construct;

(7) producing chimeric filovirus GP proteins by culturing the cells under conditions such that the DNA fragment is expressed and the chimeric protein is produced;

(8) a vaccine for more than one filovirus comprising viral particles containing one or more replicon RNA encoding chimeric GP from one or more filovirus;

(9) vaccines against Ebola and Marburg virus infections comprising a chimeric GP protein above, of infectious alphavirus particles produced from replicating RNA produced from the construct above;

(10) a pharmaceutical composition comprising a chimeric peptide encoded by any of the DNA sequences above, in a pharmaceutical carrier and/or adjuvant;

(11) a bivalent filovirus vaccine antigen comprising a chimeric GP protein comprising GP1 or its portion, from a first filovirus and GP2 or its portion from a second filovirus, where the antigen is able to elicit an immune response to 2 filoviruses in a subject; and

(12) a multivalent filovirus vaccine antigen comprising a chimeric GP protein where GP1 and GP2 are comprised of portions of GP1 and GP2 from different filoviruses, where the antigen able to elicit an immune response to more than 2 filoviruses in a subject.

ACTIVITY - Virucide. No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The chimeric filovirus GP protein is useful for inducing an immune response against infection of different filoviruses, specifically against both Ebola and Marburg viruses.

ADVANTAGE - The single-component bivalent vaccine comprising the chimeric filovirus GP protein is cost-effective, easy to produce, develop and test, and provides a protective immune response to multiple filovirus agents in a single component.
Dwg.0/10

```
=> e hevey m c/in
E1          1     HEVESSY J/IN
E2          1     HEVESY A/IN
E3          2 --> HEVEY M C/IN
E4          1     HEVEY M O/IN
E5          1     HEVEY M R/IN
E6          6     HEVEY R C/IN
E7          1     HEVEY S J/IN
E8          1     HEVEZI J M/IN
E9          5     HEVEZI P/IN
E10         2     HEVEZI P A/IN
E11         2     HEVIA A/IN
E12         2     HEVIA C R/IN

=> s e3
L9          2 "HEVEY M C"/IN

=> s l9 not l8
L10         1 L9 NOT L8

=> d l10,bib,ab
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L10 ANSWER 1 OF 1 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2000-160676 [14] WPIDS
CR 2000-160677 [14]
DNC C2000-050163
TI Novel Marburg virus vaccines used to induce an immune response against the infection in nonhuman primates.
DC B04 D16
IN **HEVEY, M C**; NEGLEY, D L; PUSHKO, P; SCHMALJOHN, A L; SMITH, J F
PA (USME-N) US MEDICAL RES INST INFECTIOUS DISEASES; (HEVE-I) HEVEY M C;

```
     SMITH J F; (USSA) US SEC OF ARMY
CYC  82
PI   WO 2000000616   A2 20000106 (200014)* EN   57
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ UG ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
            GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK
            MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US
            UZ VN YU ZW
     AU 9947090      A  20000117 (200026)
     EP 1092031      A2 20010418 (200123)  EN
         R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
     US 6517842      B1 20030211 (200314)
     US 2003152590   A1 20030814 (200355)
     AU 767551       B  20031113 (200381)
ADT  WO 2000000616 A2 WO 1999-US14174 19990621; AU 9947090 A AU 1999-47090
     19990621; EP 1092031 A2 EP 1999-930580 19990621, WO 1999-US14174 19990621;
     US 6517842 B1 Provisional US 1998-91403P 19980629, US 1999-336910
     19990621; US 2003152590 A1 Provisional US 1998-91403P 19980629, Div ex US
     1999-336910 19990621, US 2002-267322 20021009; AU 767551 B AU 1999-47090
     19990621
FDT  AU 9947090 A Based on WO 2000000616; EP 1092031 A2 Based on WO 2000000616;
     US 2003152590 A1 Div ex US 6517842; AU 767551 B Previous Publ. AU 9947090,
     Based on WO 2000000616
PRAI US 1998-91403P       19980629; US 1999-336910       19990621;
     US 2002-267322       20021009
AB   WO 200000616 A UPAB: 20031216
     NOVELTY - Marburg virus (MBGV) vaccines are new.
          DETAILED DESCRIPTION - A novel recombinant DNA construct (I)
     comprises a vector, and at least one copy of the MBGV DNA fragments
     encoding GP, NP, VP40, VP35, VP30, VP24 and GP Delta TM proteins.
          INDEPENDENT CLAIMS are also included for the following:
          (1) self-replicating RNA produced from (I);
          (2) a composition comprising infectious alphavirus particles of (1)
     in a carrier and/or adjuvant;
          (3) a host cell transformed with (I);
          (4) producing MBGV proteins by culturing the host cells of (3) to
     express the DNA fragment and ptoduce the protein;
          (5) a vaccine for MBGV, comprising viral particles containing one or
     more replicon RNAs encoding one or more GP, NP, VP40, VP35, VP30, VP24 and
     GP Delta TM proteins;
          (6) a composition, comprising one or more recombinant DNA constructs
     chosen from pRep Mus GP, pRep Mus NP, pRep Mus VP40, pRep Mus VP35, pRep
     Mus VP30, pRep Mus VP24 or pRep Mus GP Delta TM, in a carrier and/or
     adjuvant.
          USE - The replicons and vectors and constructs are used to produce
     vaccines against Marburg virus (MBGV) infection (Marburg hemorrhagic
     fever) in mammals, to elicit immune responses against MBGV antigens, to
     confer protective immunity, and to reduce disease symptoms and reduce the
     severity of disease.
          ADVANTAGE - The vaccine is efficient in protecting humans against
     MBGV.
     Dwg.0/12


=> e schmaljohn a l/in
E1            1     SCHMALJOHANN R/IN
E2            1     SCHMALJOHN A/IN
E3            8 --> SCHMALJOHN A L/IN
E4            2     SCHMALJOHN C/IN
E5           11     SCHMALJOHN C S/IN
E6            4     SCHMALKUCH J/IN
E7            4     SCHMALKUCHE C/IN
E8            4     SCHMALKUCHE J/IN
E9            3     SCHMALL D/IN
E10           2     SCHMALL G/IN
E11           1     SCHMALL G K/IN
E12          12     SCHMALL J/IN

=> s e2 or e3
              1 "SCHMALJOHN A"/IN
              8 "SCHMALJOHN A L"/IN
L11           9 "SCHMALJOHN A"/IN OR "SCHMALJOHN A L"/IN

=> s l11 not l8
L12           8 L11 NOT L8

=> s l12 not l9
L13           7 L12 NOT L9

=> s l13 and (filovir? or marburg or ebola)
            141 FILOVIR?
```

282 EBOLA
L14 5 L13 AND (FILOVIR? OR MARBURG OR EBOLA)

=> d l14,bib,ab,1-5

L14 ANSWER 1 OF 5 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2005-809991 [82] WPIDS
CR 2003-441461 [41]
DNC C2005-249028
TI New **filovirus** virus-like particle (VLP) comprising **filovirus** envelope glycoprotein (GP) and **filovirus** matrix protein (VP40), useful in preparing a vaccine against **Ebola** or **Marburg** virus infection.
DC B04 D16
IN AMAN, M J; BAVARI, S; **SCHMALJOHN, A L**; SWENSON, D; WARFIELD, K L
PA (AMAN-I) AMAN M J; (BAVA-I) BAVARI S; (SCHM-I) SCHMALJOHN A L; (SWEN-I) SWENSON D; (WARF-I) WARFIELD K L
CYC 1
PI US 2005266023 A1 20051201 (200582)* 45
ADT US 2005266023 A1 Provisional US 2001-338936P 20011107, CIP of US 2002-289839 20021107, Provisional US 2004-562800P 20040413, Provisional US 2004-562801P 20040413, US 2005-105031 20050413
PRAI US 2005-105031 20050413; US 2001-338936P 20011107;
US 2002-289839 20021107; US 2004-562800P 20040413;
US 2004-562801P 20040413
AB US2005266023 A UPAB: 20051222
NOVELTY - A new **filovirus** virus-like particle (VLP) comprising **filovirus** envelope glycoprotein (GP) and **filovirus** matrix protein, VP40 is produced by expressing in a cell a polynucleotide encoding **filovirus** envelope GP and VP40 so that the polynucleotide is expressed and the VLP is produced.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) inhibiting the association of a **filovirus** envelope GP with lipid rafts;

(2) preventing **filovirus** trafficking into and out of a cell which comprises disrupting lipid rafts of the cell;

(3) preventing **filovirus** trafficking;

(4) a **filovirus** vaccine comprising the VLP and a nucleic acid encoding an agent capable of eliciting an immune response against the **filovirus**;

(5) introducing an agent into a cell;

(6) an **Ebola** VLP-producing cell comprising a mammalian cell expressing **Ebola** GP and VP40;

(7) testing an agent involved in **filovirus** budding;

(8) inhibiting **Ebola** virus infection in a cell;

(9) detecting **Ebola** virus infection;

(10) a kit for detecting **Ebola** or **Marburg** virus infection comprising **Ebola** or **Marburg** VLPs;

(11) detecting **Marburg** virus infection;

(12) a kit for testing agents involved in **Ebola** budding the kit comprising a cell producing **Ebola** VLPs and ancillary reagents for detecting VLPs in the supernatant of the cells when cells are cultured;

(13) a **Marburg** VLP-producing cell comprising a mammalian cell expressing **Marburg** GP and VP40;

(14) a kit for testing agents involved in **Marburg** budding the kit comprising a cell producing **Marburg** VLPs and ancillary reagents for detecting VLPs in the supernatant of the cells when cells are cultured;

(15) an immunogenic composition comprising, in a physiologically acceptable vehicle, **Ebola** or **Marburg** VLPs;

(16) stimulating an **Ebola** virus specific immune response;

(17) stimulating a **Marburg** virus specific immune response;

(18) a panfilovirus vaccine comprising a mixture of **Ebola** virus (EBOV) and **Marburg** virus (MARV) VLPs; and

(19) a MARV vaccine protective against infection with MARV-Musoke, MARV-Ravn, and MARV-Ci67, comprising MARV VLPs consisting essentially of GP and VP40 from MARV-Musoke.

ACTIVITY - Virucide.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The **filovirus** virus-like particle (VLP) is useful in preparing a vaccine against **Ebola** or **Marburg** virus infection.
Dwg.0/21

L14 ANSWER 2 OF 5 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2003-441461 [41] WPIDS
CR 2005-809991 [82]
DNC C2003-116869
TI New **filovirus** virus-like particle having an envelope glycoprotein and matrix protein, useful for diagnosing, preventing and/or treating **Ebola** and **Marburg** virus infections in humans and non-human primates.
DC B04 D16

PA (USSA) US ARMY MEDICAL RES INST INFECTIOUS DISE; (AMAN-I) AMAN M J; (BAVA-I) BAVARI S; (SCHM-I) SCHMALJOHN A L
CYC 85
PI WO 2003039477 A2 20030515 (200341)* EN 61
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
US 2004057967 A1 20040325 (200422)
EP 1461424 A2 20040929 (200463) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
AU 2002352546 A1 20030519 (200464)
ADT WO 2003039477 A2 WO 2002-US35834 20021107; US 2004057967 A1 Provisional US 2001-338936P 20011107, US 2002-289839 20021107; EP 1461424 A2 EP 2002-789508 20021107, WO 2002-US35834 20021107; AU 2002352546 A1 AU 2002-352546 20021107
FDT EP 1461424 A2 Based on WO 2003039477; AU 2002352546 A1 Based on WO 2003039477
PRAI US 2001-338936P 20011107; US 2002-289839 20021107
AB WO2003039477 A UPAB: 20051222

NOVELTY - A new **filovirus** virus-like particle (VLP) comprises **filovirus** envelope glycoprotein (GP), and **filovirus** matrix protein (VP40), and is produced by expressing in a cell a polynucleotide encoding GP and VP40, such that the polynucleotide is expressed and VLP is produced.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for inhibiting the association of GP with lipid rafts, comprising inhibiting palmitoylation at cysteine residues 670 and 672 of the GP;

(2) a method for preventing **filovirus** trafficking into and out of a cell comprising disrupting lipid rafts of the cell or introducing cholesterol synthesis inhibitors to a cell;

(3) a **filovirus** vaccine comprising VLP and/or a nucleic acid encoding an agent capable of eliciting an immune response against the **filovirus**;

(4) a method for introducing an agent into a cell, comprising packaging the agent into a VLP producing a packed VLP and allowing the packed VLP to enter the cell;

(5) a method for testing an agent involved in **filovirus** budding, comprising introducing the agent to a cultured cell producing **filovirus** VLP and monitoring the presence or absence of a change in the budding of VLP as compared to a control by measuring VLPs in supernatant of the cultured cell, where a reduction or increase in the number of VLP in the supernatant indicates a negative or positive agent, respectively, on **filovirus** budding;

(6) a method for inhibiting **Ebola** virus infection in a cell, comprising administering raft-disrupting agents to the cell lipid;

(7) a method for detecting **Ebola** virus infection comprising contacting a sample from a subject suspected of having **Ebola** virus infection with an **Ebola** VLP, and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Ebola** VLP and antibodies specific for it in the sample;

(8) a kit for the detection of **Ebola** virus infection comprising **Ebola** VLPs;

(9) a method for detecting **Marburg** virus infection comprising contacting a sample from a subject suspected of having **Marburg** virus infection with a **Marburg** VLP, and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Marburg** VLP and antibodies specific for it in the sample;

(10) a kit for the detection of **Marburg** virus infection comprising **Marburg** VLPs;

(11) a kit for testing agents involved in **Ebola** or **Marburg** budding, comprising a cell producing **Ebola** or **Marburg** VLPs and ancillary reagents for detecting VLPs in the supernatant of the cells when cells are cultured;

(12) an **Ebola** VLP-producing or **Marburg** VLP-producing cell comprising a mammalian cell expressing **Ebola** GP or **Marburg** GP, and VP40;

(13) an immunogenic composition comprising **Ebola** or **Marburg** VLPs in a vehicle; and

(14) a method for stimulating an **Ebola** or **Marburg** virus specific immune response, comprising administering to a subject an **Ebola** or **Marburg** VLPs in a vehicle.

ACTIVITY - Virucide.

Test details are described but nor results were given.

MECHANISM OF ACTION - Vaccine.

USE - The methods and compositions of the present invention of generating genome-free **Ebola** and/or **Marburg** VLPs, are useful for diagnosing, preventing and/or treating **Ebola** and **Marburg** virus

Dwg.0/9

L14 ANSWER 3 OF 5 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2001-280564 [29] WPIDS
DNC C2001-085063
TI Inducing an immune response to a **Marburg** or **Ebola** virus involves delivering a genetic vaccine, which contains a genetic construct encoding antigenic determinants for **filovirus**, using a particle acceleration device.
DC B04 D16
IN FULLER, D L; HAYNES, J R; JAHRLING, P B; **SCHMALJOHN, A**; SCHMALJOHN, C S
PA (POWD-N) POWDERJECT VACCINES INC
CYC 1
PI US 6200959 B1 20010313 (200129)* 33
ADT US 6200959 B1 US 1996-760615 19961204
PRAI US 1996-760615 19961204
AB US 6200959 B UPAB: 20010528
NOVELTY - Inducing an immune response to a **Marburg** or **Ebola** virus glycoprotein in a mammal comprises delivering the foreign genetic construction, which comprises a promoter operative in cells of the mammal and a coding region for a determinant of the glycoprotein, into the epidermis of the mammal using a particle acceleration device.

DETAILED DESCRIPTION - Inducing an immune response to a **Marburg** or **Ebola** virus glycoprotein in a mammal comprises:

(a) providing a genetic construction comprising a promoter operative in cells of the mammal and a coding region for a determinant of the glycoprotein, the genetic construction not comprising sequences necessary for replication of the virus;

(b) coating copies of the genetic construction onto carrier particles small in size in relation to the size of the cells of the mammal; and

(c) accelerating the coated carrier particles into epidermal cells of the mammal in vivo, thus inducing an immune response against the glycoprotein.

An INDEPENDENT CLAIM is also included for a composition of matter comprising a carrier particle and a genetic construction coated onto the carrier particle, where the genetic construction comprises a promoter operative in the cells of a mammal and a coding region for a determinant of a **Marburg** or **Ebola** virus glycoprotein.

ACTIVITY - Antiviral. Twenty Balb/C mice were vaccinated twice with the genetic construct encoding the **Ebola** glycoprotein, six weeks apart (2 targets per dose, 400 psi). Twenty additional Balb/C mice were vaccinated three times using the same genetic construct, four weeks apart. Seventeen control mice were not immunized. All of the control mice died within a week. No significant difference in survival was observed between the mice that received two vaccinations and those that received three. In either case, 70-75 % of the mice survived **Ebola** virus challenge.

MECHANISM OF ACTION - Vaccine.

USE - The method is useful for inducing a protective immune response to a **Marburg** or **Ebola** virus (claimed). In particular, the method is useful for inducing humoral, cell-mediated and secretory immune responses in the treated individual.

ADVANTAGE - Unlike prior methods, the present method is capable of producing cytotoxic immunity, immunological memory, and humoral (circulating) antibodies, without having any unacceptable risk of pathogenecity, or mutation or recombination of the virus in the vaccinated individual. The method is also inherently safe, is not painful to administer and does not require growth or use of **filoviruses**, which may be spread by aerosol transmission and are typically fatal.
Dwg.0/8

L14 ANSWER 4 OF 5 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2001-235096 [24] WPIDS
DNN N2001-168082 DNC C2001-070459
TI Novel monoclonal antibody against epitopes on the **Ebola** virus glycoprotein useful as vaccines for detection, prevention and/or therapeutical treatment of **Ebola** virus infections.
DC B04 D16 S03
IN HART, M K; **SCHMALJOHN, A L**; WILSON, J A
PA (USSA) US ARMY MEDICAL RES INST INFECTIOUS DISE; (USSA) US SEC OF ARMY
CYC 83
PI WO 2001016183 A1 20010308 (200124)* EN 62
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 2000070896 A 20010326 (200137)
US 6630144 B1 20031007 (200374)
ADT WO 2001016183 A1 WO 2000-US23790 20000829; AU 2000070896 A AU 2000-70896

2000-650086 20000829
FDT AU 2000070896 A Based on WO 2001016183
PRAI US 1999-151505P 19990830; US 2000-650086 20000829
AB WO 200116183 A UPAB: 20010502
NOVELTY - An antibody (I) which recognizes **Ebola** virus glycoprotein (EVGP), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an antibody (II) which competes with (I) for binding to EVGP;

(2) a mixture (III) comprising **Ebola** virus antibodies comprising antibodies produced by hybridomas EGP 13F6-1-2 accession no. PTA 373, EGP 6D3-1-1 accession no. PTA 374, EGP 13C6-1-1 accession no. PTA 375, EGP 6D8-1-2 accession no. PTA 376, and/or EGP 12B5-1-1 accession no. PTA 436;

(3) a therapeutic composition (C) for ameliorating symptoms of **Ebola** virus infection, comprising (III);

(4) a passive vaccine against **Ebola** virus infection comprising (III);

(5) a monoclonal antibody producing cell line that produces (I);

(6) an anti-**Ebola** composition, comprising (I);

(7) a kit for detecting **Ebola** virus in a biological sample, comprising a container holding MAb 13F6, MAb 6D3, MAb 13C6, MAb 6D8, and/or MAb 12B5, and instructions for use;

(8) a vaccine for **Ebola** virus comprising one or more antigenic peptide epitopes recognized by MAb;

(9) a pharmaceutical composition comprising a peptide encoded by a 105 or 295 residue amino acid sequence (S1), fully defined in the specification, or a sequence (S2);

(10) an antiidiotypic antibody (IV) produced from MAb or (II); and

(11) an **Ebola** virus vaccine comprising (IV).

(S2) is AlaThrGlnValGluGlnHisHisArgArgThrAspAsnAspSerThrAla, GluGlnHisHisArgArgThrAspAsn, HisAsnThrProValTyrLysLeuAspIleSerGluAlaThrGlnValGlu, ValTyrLysLeuAspIleSerGluAla, GlyLysLeuGlyLeuIleThrAsnThrIleAlaGlyValAlaGlyLeuIle, or LeuIleThrAsnThrIleAlaGlyVal.

ACTIVITY - Antiviral.

MECHANISM OF ACTION - Vaccine.

Protective efficacy of (I) was determined by evaluating purified monoclonal antibodies for their ability to protect BALB/c mice from a lethal **Ebola** challenge. Groups of 5 mice/experiment were injected intraperitoneally with 100, 50 and 25 micro g of (I) in phosphate buffered saline, 1 day before, or 1 or 2 days after challenge with 300 times the lethal dose for 50 % adult mice (10 plaque forming units). All the monoclonal antibodies demonstrated protective efficacy when administered 1 day prior to or after challenge.

USE - (III) is useful for preventing **Ebola** virus infection in a subject. (I) is useful for inhibiting and ameliorating symptoms of **Ebola** virus infection. (I) is useful for detecting **Ebola** virus in a sample, by incubating the sample with (I), and detecting the complex, the presence or absence of the complex indicates the presence or absence of **Ebola** virus in the sample. (I) is also useful for treating **Ebola** virus infection. (All claimed).
Dwg.0/2

L14 ANSWER 5 OF 5 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2000-160677 [14] WPIDS
CR 2000-160676 [14]; 2005-233265 [24]
DNN N2000-119889 DNC C2000-050164
TI New GP, NP, VP24, VP30, VP35 and VP40 **Ebola** virus proteins, useful for prevention, treatment or diagnosis of **Ebola** infection, particularly where expressed from virus replicons.
DC B04 D16 S03
IN HART, M K; PUSHKO, P; **SCHMALJOHN, A L**; SMITH, J F; WILSON, J A; BAILEY, M A; OLINGER, G G
PA (USME-N) US MEDICAL RES INST INFECTIOUS DISEASES; (HART-I) HART M K; (PUSH-I) PUSHKO P; (SCHM-I) SCHMALJOHN A L; (SMIT-I) SMITH J F; (WILS-I) WILSON J A; (BAIL-I) BAILEY M A; (OLIN-I) OLINGER G G; (USSA) US SEC OF ARMY
CYC 87
PI WO 2000000617 A2 20000106 (200014)* EN 70
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
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AU 9950844 A 20000117 (200026)
EP 1119627 A2 20010801 (200144) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2002164582 A1 20021107 (200275)
US 2003224015 A1 20031204 (200380)
AU 767147 B 20031030 (200382)
US 2004146859 A1 20040729 (200450)
US 6984504 B2 20060110 (200604)

19990622; EP 1119627 A2 EP 1999-935350 19990622, WO 1999-US14311 19990622; US 2002164582 A1 Provisional US 1998-91403P 19980629, US 1999-337946 19990622; US 2003224015 A1 Provisional US 1998-91403P 19980629, CIP of US 1999-337946 19990622, US 2003-384976 20030310; AU 767147 B AU 1999-50844 19990622; US 2004146859 A1 Provisional US 1998-91403P 19980629, Cont of US 1999-337946 19990622, US 2003-696633 20031029; US 6984504 B2 Provisional US 1998-91403P 19980629, Cont of US 1999-337946 19990622, US 2003-696633 20031029

FDT AU 9950844 A Based on WO 2000000617; EP 1119627 A2 Based on WO 2000000617; AU 767147 B Previous Publ. AU 9950844, Based on WO 2000000617

PRAI US 1998-91403P 19980629; US 1999-337946 19990622; US 2003-384976 20030310; US 2003-696633 20031029

AB WO 200000617 A UPAB: 20060116

NOVELTY - GP, NP, VP24, VP30, VP35 and VP40 **Ebola** virus proteins (or their immunologically identifiable portions) comprising sequences (I)-(VII) (where VP30 can be encoded by sequences (IV) and/or (V)) of 251-739 amino acids (aa), are new (all sequences are fully defined in the specification).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) DNA sequences (VIII)-(XIV) of 847-2428 nucleotides (nt), or their fragments of at least 15 nt and/or which encode at least 5 aa of sequences (I)-(VII), encoding a GP, NP, VP24, VP30, VP35 or VP40 **Ebola** virus protein (where VP30 can be encoded by (XI) and/or (XIV));

(2) a recombinant DNA construct (A) containing, in a vector, at least one of sequences (VIII)-(XIV) or their fragments of at least 15 nt;

(3) self-replicating RNA (B) produced by any one of EboVP24ReP, EboVP30ReP, EboVP35ReP, EboVP40ReP, EboVPNPReP, EboVPGPReP or EboVP30ReP (constructs of (A));

(4) infectious alphavirus particles (C) produced by packaging (B);

(5) prokaryotic/eukaryotic host cells (D) transformed with (A);

(6) production of **Ebola** virus proteins by culturing (D);

(7) antibodies (Ab) (E) raised against peptides of sequences (I)-(VII) and sequences of 11 and 23 amino acids (XV)-(XVI) respectively;

(8) detecting **Ebola** virus infection by formation of immune complex with (E);

(9) detecting **Ebola** GP RNA by polymerase chain reaction (PCR), using primers derived from (VIII);

(10) a diagnostic kit (F) for **Ebola** infection comprising fragments of at least 12 consecutive nt from (VIII) specific for the amplification of DNA or RNA of **Ebola** virus by PCR amplification plus ancillary reagents for detection; and

(11) a vaccine comprising (C);

All sequences are fully defined in the specification

ACTIVITY - Antiviral.

Capped replicon RNAs, from **Ebola** protein VP24, were produced by in vitro T7 run-off transcription of linearized plasmids and used, together with two helper RNAs expressing the structural proteins of Venezuelan equine encephalitis (VEE) virus, to transfect baby hamster kidney cells. Recombinant VEE virus replicons were recovered from the culture supernatant by centrifugation through a 20% sucrose solution. Balb/c mice were injected twice with 2 million focus-forming units of the resulting replicons (designated EboVP24VRP), then 1 month after the second injection challenged with 105 plaque-forming units of mouse-adated **Ebola** virus. All animals survived the challenge, compared with none of unvaccinated controls. Another example shows that immune serum from animals vaccinated with a replicon based on the GP protein (but not those based on other **Ebola** proteins) passively protected unvaccinated mice against challenge.

MECHANISM OF ACTION - Vaccine.

USE - (A) are useful to produce the following:

(1) the **Ebola** virus proteins as described above;

(2) self-replicating RNA; or

(3) infectious alphavirus particles;

all of which (also the constructs themselves) are useful in pharmaceutical compositions and protective vaccines. The **Ebola** proteins are also useful for the diagnosis of **Ebola** infection (by detecting antibodies) and for raising specific antibodies (E), which can be used to detect the proteins. DNA sequences (VIII)-(XIV) are useful as probes and primers for diagnostic hybridization or polymerase chain reaction assays for detecting **Ebola** virus (all claimed).

Dwg.0/4

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	40.09	74.45

FILE 'MEDLINE' ENTERED AT 10:41:26 ON 06 MAR 2006

FILE LAST UPDATED: 4 MAR 2006 (20060304/UP). FILE COVERS 1950 TO DATE.

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 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> e grogan c c/au
E1             6     GROGAN C/AU
E2             1     GROGAN C B/AU
E3             1 --> GROGAN C C/AU
E4            12     GROGAN C H/AU
E5             3     GROGAN C K/AU
E6             9     GROGAN C M/AU
E7             1     GROGAN CASE/AU
E8             1     GROGAN CASE C/AU
E9             1     GROGAN CLARE/AU
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E12            6     GROGAN D/AU

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               1 "GROGAN C C"/AU
L15            7 "GROGAN C"/AU OR "GROGAN C C"/AU

=> d l15,ti,1-7

L15  ANSWER 1 OF 7     MEDLINE on STN
TI   Characterisation of an antibody coated microcantilever as a potential
     immuno-based biosensor.

L15  ANSWER 2 OF 7     MEDLINE on STN
TI   Sendai virus wild-type and mutant C proteins show a direct correlation
     between L polymerase binding and inhibition of viral RNA synthesis.

L15  ANSWER 3 OF 7     MEDLINE on STN
TI   A specialized mental health plan for persons with severe mental illness
     under managed competition.

L15  ANSWER 4 OF 7     MEDLINE on STN
TI   The structure and characteristics of rural hospital consortia.

L15  ANSWER 5 OF 7     MEDLINE on STN
TI   A highly sensitive, nonradioactive DNA labeling and detection system.

L15  ANSWER 6 OF 7     MEDLINE on STN
TI   Changing physician behavior: does medical review of Part B Medicare claims
     make a difference?.

L15  ANSWER 7 OF 7     MEDLINE on STN
TI   Evaluating rural hospital consortia.

=> e hevey m c/au
E1             1     HEVEY L A/AU
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E4             3     HEVEY MICHAEL/AU
E5             1     HEVEY MICHAEL C/AU
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E7             4     HEVEY R C/AU
E8             1     HEVEZ A/AU
E9             4     HEVEZI J/AU
E10           12     HEVEZI J M/AU
E11            1     HEVEZI JAMES/AU
E12            6     HEVEZI JAMES M/AU

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=> s l15 and (filovir? or ebola or marburg)
          246 FILOVIR?
          986 EBOLA
         1120 MARBURG
L17         0 L15 AND (FILOVIR? OR EBOLA OR MARBURG)

=> e schmaljohn a l/au
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E3           22 --> SCHMALJOHN A L/AU
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E6           24      SCHMALJOHN C/AU
E7           52      SCHMALJOHN C S/AU
E8            6      SCHMALJOHN CONNIE/AU
E9            8      SCHMALJOHN CONNIE S/AU
E10           1      SCHMALL A/AU
E11          28      SCHMALL B/AU
E12           1      SCHMALL BAUER W/AU

=> s e2-e5
            8 "SCHMALJOHN A"/AU
           22 "SCHMALJOHN A L"/AU
            8 "SCHMALJOHN ALAN"/AU
            4 "SCHMALJOHN ALAN L"/AU
L18        42 ("SCHMALJOHN A"/AU OR "SCHMALJOHN A L"/AU OR "SCHMALJOHN ALAN"/A
              U OR "SCHMALJOHN ALAN L"/AU)

=> s l18 and (filovir? or ebola or marburg)
          246 FILOVIR?
          986 EBOLA
         1120 MARBURG
L19        18 L18 AND (FILOVIR? OR EBOLA OR MARBURG)

=> d l19,cbib,ab,1-18
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L19 ANSWER 1 OF 18 MEDLINE on STN
2005180140. PubMed ID: 15811650. Virus-like particles exhibit potential as a pan-**filovirus** vaccine for both **Ebola** and **Marburg** viral infections. Swenson Dana L; Warfield Kelly L; Negley Diane L; **Schmaljohn Alan**; Aman M Javad; Bavari Sina. (United States Army Medical Research Institute of Infectious Diseases, 1425 Porter Street, Frederick, MD 21702-5011, USA.. dana.swenson@det.amedd.army.mil) . Vaccine, (2005 Apr 27) Vol. 23, No. 23, pp. 3033-42. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.

AB A safe and effective pan-**filovirus** vaccine is highly desirable since the **filoviruses Ebola** virus (EBOV) and **Marburg** virus (MARV) cause highly lethal disease typified by unimpeded viral replication and severe hemorrhagic fever. Previously, we showed that expression of the homologous glycoprotein (GP) and matrix protein VP40 from a single **filovirus**, either EBOV or MARV, resulted in formation of wild-type virus-like particles (VLPs) in mammalian cells. When used as a vaccine, the wild-type VLPs protected from homologous **filovirus** challenge. The aim of this work was to generate a multi-agent vaccine that would simultaneously protect against multiple and diverse members of the **Filoviridae** family. Our initial approach was to construct hybrid VLPs containing heterologous viral proteins, of EBOV and MARV, and test the efficacy of the hybrid VLPs in a guinea pig model. Our data indicate that vaccination with GP was required and sufficient to protect against a homologous **filovirus** challenge, as heterologous wild-type VLPs or hybrid VLPs that did not contain the homologous GP failed to protect. Alternately, we vaccinated guinea pigs with a mixture of wild-type **Ebola** and **Marburg** VLPs. Vaccination with a single dose of the multivalent VLP vaccine elicited strong immune responses to both viruses and protected animals against EBOV and MARV challenge. This work provides a critical foundation towards the development of a pan-**filovirus** vaccine that is safe and effective for use in primates and humans.

L19 ANSWER 2 OF 18 MEDLINE on STN
2004405253. PubMed ID: 15308377. **Marburg** virus-like particles protect guinea pigs from lethal **Marburg** virus infection. Warfield Kelly L; Swenson Dana L; Negley Diane L; **Schmaljohn Alan L**; Aman M Javad; Bavari Sina. (United States Army Medical Research Institute of Infectious Diseases, 1425 Porter Street, Frederick, MD 21702-5011, USA.. kelly.warfield@det.amedd.army.mil) . Vaccine, (2004 Sep 3) Vol. 22, No. 25-26, pp. 3495-502. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.

AB Ongoing outbreaks of **filoviruses** in Africa and concerns about their use

effective vaccines to prevent the high mortality associated with these viruses. We previously reported the generation of virus-like particles (VLPs) for the **filoviruses, Marburg** (MARV) and **Ebola** (EBOV) virus, and that vaccinating mice with **Ebola** VLPs (eVLPs) results in complete survival from a lethal EBOV challenge. The objective of this study was to determine the efficacy of **Marburg** VLPs (mVLPs) as a potential vaccine against lethal MARV infection in a guinea pig model. Guinea pigs vaccinated with mVLPs or inactivated MARV developed MARV-specific antibody titers, as tested by ELISA or plaque-reduction and neutralization assays and were completely protected from a MARV challenge over 2000 LD50. While eVLP vaccination induced high EBOV-specific antibody responses, it did not cross-protect against MARV challenge in guinea pigs. Vaccination with mVLP or eVLP induced proliferative responses in vitro only upon re-exposure to the homologous antigen and this recall proliferative response was dependent on the presence of CD4+ T cells. Taken together with our previous work, these findings suggest that VLPs are a promising vaccine candidate for the deadly **filovirus** infections.

L19 ANSWER 3 OF 18 MEDLINE on STN
2004034503. PubMed ID: 14734183. Generation of **Marburg** virus-like particles by co-expression of glycoprotein and matrix protein. Swenson Dana L; Warfield Kelly L; Kuehl Kathleen; Larsen Thomas; Hevey Michael C; **Schmaljohn Alan**; Bavari Sina; Aman M Javad. (U.S. Army Medical Research Institute of Infectious Diseases, 1425 Porter Street, Frederick, MD 21702, USA.) FEMS immunology and medical microbiology, (2004 Jan 15) Vol. 40, No. 1, pp. 27-31. Journal code: 9315554. ISSN: 0928-8244. Pub. country: Netherlands. Language: English.

AB **Marburg** virus (MARV), the causative agent of a severe hemorrhagic fever, has a characteristic filamentous morphology. Here we report that co-expression of MARV glycoprotein and matrix protein (VP40) in mammalian cells leads to spontaneous budding of filamentous particles strikingly similar to wild-type MARV. In addition, these particles elicit an immune response in BALB/c mice. The generation of non-replicating **Marburg** virus-like particles (VLPs) should significantly facilitate the research on molecular mechanisms of MARV assembly and release. Furthermore, VLPs may be an excellent vaccine candidate against **Marburg** infection.

L19 ANSWER 4 OF 18 MEDLINE on STN
2003611193. PubMed ID: 14673108. **Ebola** virus-like particles protect from lethal **Ebola** virus infection. Warfield Kelly L; Bosio Catharine M; Welcher Brent C; Deal Emily M; Mohamadzadeh Mansour; **Schmaljohn Alan**; Aman M Javad; Bavari Sina. (US Army Medical Research Institute of Infectious Diseases, Frederick, MD 21702, USA.) Proceedings of the National Academy of Sciences of the United States of America, (2003 Dec 23) Vol. 100, No. 26, pp. 15889-94. Electronic Publication: 2003-12-12. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The **filovirus Ebola** causes hemorrhagic fever with 70-80% human mortality. High case-fatality rates, as well as known aerosol infectivity, make **Ebola** virus a potential global health threat and possible biological warfare agent. Development of an effective vaccine for use in natural outbreaks, response to biological attack, and protection of laboratory workers is a higher national priority than ever before. Coexpression of the **Ebola** virus glycoprotein (GP) and matrix protein (VP40) in mammalian cells results in spontaneous production and release of virus-like particles (VLPs) that resemble the distinctively filamentous infectious virions. VLPs have been tested and found efficacious as vaccines for several viruses, including papillomavirus, HIV, parvovirus, and rotavirus. Herein, we report that **Ebola** VLPs (eVLPs) were immunogenic in vitro as eVLPs matured and activated mouse bone marrow-derived dendritic cells, assessed by increases in cell-surface markers CD40, CD80, CD86, and MHC class I and II and secretion of IL-6, IL-10, macrophage inflammatory protein (MIP)-1alpha, and tumor necrosis factor alpha by the dendritic cells. Further, vaccinating mice with eVLPs activated CD4+ and CD8+ T cells, as well as CD19+ B cells. After vaccination with eVLPs, mice developed high titers of **Ebola** virus-specific antibodies, including neutralizing antibodies. Importantly, mice vaccinated with eVLPs were 100% protected from an otherwise lethal **Ebola** virus inoculation. Together, our data suggest that eVLPs represent a promising vaccine candidate for protection against **Ebola** virus infections and a much needed tool to examine the genesis and nature of immune responses to **Ebola** virus.

L19 ANSWER 5 OF 18 MEDLINE on STN
2003558785. PubMed ID: 14639532. **Ebola** and **Marburg** viruses replicate in monocyte-derived dendritic cells without inducing the production of cytokines and full maturation. Bosio Catharine M; Aman M Javad; Grogan Case; Hogan Robert; Ruthel Gordon; Negley Diane; Mohamadzadeh Mansour; Bavari Sina; **Schmaljohn Alan**. (United States Army Medical Research Institute of Infectious Diseases, Frederick, Maryland 21702-5011, USA.) The Journal of infectious diseases, (2003 Dec 1) Vol. 188, No. 11, pp. 1630-8. Electronic Publication: 2003-11-14. Journal code: 0413675. ISSN:

AB Ebola virus (EBOV) and Marburg virus (MARV) cause rapidly progressive hemorrhagic fever with high mortality and may possess specialized mechanisms to evade immune destruction. We postulated that immune evasion could be due to the ability of EBOV and MARV to interfere with dendritic cells (DCs), which link innate and adaptive immune responses. We demonstrate that EBOV and MARV infected and replicated in primary human DCs without inducing cytokine secretion. Infected DC cultures supported exponential viral growth without releasing interferon (IFN)-alpha and were impaired in IFN-alpha production if treated with double-stranded RNA. Moreover, EBOV and MARV impaired the ability of DCs to support T cell proliferation, and infected, immature DCs underwent an anomalous maturation. These findings may explain the profound virulence of EBOV and MARV--DCs are disabled, and an effective early host response is delayed by the necessary reliance on less-efficient secondary mechanisms.

L19 ANSWER 6 OF 18 MEDLINE on STN
2003456270. PubMed ID: 14517087. Characterization of monoclonal antibodies to **Marburg** virus (strain Musoke) glycoprotein and identification of two protective epitopes. Hevey Michael; Negley Diane; **Schmaljohn Alan**. (Virology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 2170, USA.. michael.hevey@amedd.army.mil) . Virology, (2003 Sep 15) Vol. 314, No. 1, pp. 350-7. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.
AB Monoclonal antibodies (MAbs) reactive with **Marburg** virus (strain Musoke) were evaluated for both biological activity and specificity. Several of the **Marburg** virus- (MBGV) specific MAbs reduced the size and/or number of MBGV plaques in vitro. The ability of the MAbs to affect plaque formation in vitro was demonstrated to be specific for the glycoprotein (GP) of the strain of MBGV used for vaccination. Using deletion analysis and peptide mapping, the binding epitopes of several of these neutralizing MAbs were identified. Not unexpectedly, the epitopes were shown to lie in the most hypervariable and highly glycosylated region of MBGV GP. An analysis of the in vivo activity of several MAbs revealed that some antibodies provided substantial but incomplete protection of naive guinea pigs by passive transfer. These data suggest that neutralizing epitopes exist within MBGV GP but that induction of antibodies to these neutralizing epitopes may not be sufficient for protection from lethal infection.

L19 ANSWER 7 OF 18 MEDLINE on STN
2003386659. PubMed ID: 12922144. Comparison of individual and combination DNA vaccines for B. anthracis, **Ebola** virus, **Marburg** virus and Venezuelan equine encephalitis virus. Riemenschneider Jenny; Garrison Aura; Geisbert Joan; Jahrling Peter; Hevey Michael; Negley Diane; **Schmaljohn Alan**; Lee John; Hart Mary Kate; Vanderzanden Lorna; Custer David; Bray Mike; Ruff Albert; Ivins Bruce; Bassett Anthony; Rossi Cynthia; Schmaljohn Connie. (Virology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 21702-5011, USA.) Vaccine, (2003 Sep 8) Vol. 21, No. 25-26, pp. 4071-80. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.
AB Multiagent DNA vaccines for highly pathogenic organisms offer an attractive approach for preventing naturally occurring or deliberately introduced diseases. Few animal studies have compared the feasibility of combining unrelated gene vaccines. Here, we demonstrate that DNA vaccines to four dissimilar pathogens that are known biowarfare agents, Bacillus anthracis, **Ebola** (EBOV), **Marburg** (MARV), and Venezuelan equine encephalitis virus (VEEV), can elicit protective immunity in relevant animal models. In addition, a combination of all four vaccines is shown to be equally as effective as the individual vaccines for eliciting immune responses in a single animal species. These results demonstrate for the first time the potential of combined DNA vaccines for these agents and point to a possible method of rapid development of multiagent vaccines for disparate pathogens such as those that might be encountered in a biological attack.

L19 ANSWER 8 OF 18 MEDLINE on STN
2003262689. PubMed ID: 12787740. Molecular mechanisms of **filovirus** cellular trafficking. Aman M Javad; Bosio Catharine M; Panchal Rekha G; Burnett James C; **Schmaljohn Alan**; Bavari Sina. (Clinical Research Management Inc., 1425 Porter Street, Frederick, MD 21702, USA.. amanm@ncifcrf.gov) . Microbes and infection / Institut Pasteur, (2003 Jun) Vol. 5, No. 7, pp. 639-49. Ref: 69. Journal code: 100883508. ISSN: 1286-4579. Pub. country: France. Language: English.
AB The **filoviruses, Ebola** and **Marburg**, are two of the most pathogenic viruses, causing lethal hemorrhagic fever in humans. Recent discoveries suggest that **filoviruses**, along with other phylogenetically or functionally related viruses, utilize a complex mechanism of replication exploiting multiple cellular components including lipid rafts, endocytic compartments, and vacuolar protein sorting machinery. In this review, we summarize these recent findings and discuss the implications for vaccine

L19 ANSWER 9 OF 18 MEDLINE on STN
2002249346. PubMed ID: 11988060. Hemorrhagic fever viruses as biological weapons: medical and public health management. Borio Luciana; Inglesby Thomas; Peters C J; **Schmaljohn Alan L**; Hughes James M; Jahrling Peter B; Ksiazek Thomas; Johnson Karl M; Meyerhoff Andrea; O'Toole Tara; Ascher Michael S; Bartlett John; Breman Joel G; Eitzen Edward M Jr; Hamburg Margaret; Hauer Jerry; Henderson D A; Johnson Richard T; Kwik Gigi; Layton Marci; Lillibridge Scott; Nabel Gary J; Osterholm Michael T; Perl Trish M; Russell Philip; Tonat Kevin. (Johns Hopkins Center for Civilian Biodefense Strategies, Johns Hopkins Schools of Medicine and Public Health, 111 Market Pl, Suite 830, Baltimore, MD 21202, USA. (Working Group on Civilian Biodefense). Lborio@jhsph.edu) . JAMA : the journal of the American Medical Association, (2002 May 8) Vol. 287, No. 18, pp. 2391-405. Ref: 140. Journal code: 7501160. ISSN: 0098-7484. Pub. country: United States. Language: English.

AB OBJECTIVE: To develop consensus-based recommendations for measures to be taken by medical and public health professionals if hemorrhagic fever viruses (HFVs) are used as biological weapons against a civilian population. PARTICIPANTS: The Working Group on Civilian Biodefense included 26 representatives from academic medical centers, public health, military services, governmental agencies, and other emergency management institutions. EVIDENCE: MEDLINE was searched from January 1966 to January 2002. Retrieved references, relevant material published prior to 1966, and additional sources identified by participants were reviewed. CONSENSUS PROCESS: Three formal drafts of the statement that synthesized information obtained in the evidence-gathering process were reviewed by the working group. Each draft incorporated comments and judgments of the members. All members approved the final draft. CONCLUSIONS: Weapons disseminating a number of HFVs could cause an outbreak of an undifferentiated febrile illness 2 to 21 days later, associated with clinical manifestations that could include rash, hemorrhagic diathesis, and shock. The mode of transmission and clinical course would vary depending on the specific pathogen. Diagnosis may be delayed given clinicians' unfamiliarity with these diseases, heterogeneous clinical presentation within an infected cohort, and lack of widely available diagnostic tests., Initiation of ribavirin therapy in the early phases of illness may be useful in treatment of some of these viruses, although extensive experience is lacking. There are no licensed vaccines to treat the diseases caused by HFVs.

L19 ANSWER 10 OF 18 MEDLINE on STN
2002145489. PubMed ID: 11877482. Lipid raft microdomains: a gateway for compartmentalized trafficking of **Ebola** and **Marburg** viruses. Bavari Sina; Bosio Catharine M; Wiegand Elizabeth; Ruthel Gordon; Will Amy B; Geisbert Thomas W; Hevey Michael; Schmaljohn Connie; **Schmaljohn Alan**; Aman M Javad. (Dept. of Cell Biology and Biochemistry, U.S. Army Medical Research Institute of Infectious Diseases, Frederick, MD 21702-5011, USA.. bavaris@ncifcrf.gov) . The Journal of experimental medicine, (2002 Mar 4) Vol. 195, No. 5, pp. 593-602. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Spatiotemporal aspects of **filovirus** entry and release are poorly understood. Lipid rafts act as functional platforms for multiple cellular signaling and trafficking processes. Here, we report the compartmentalization of **Ebola** and **Marburg** viral proteins within lipid rafts during viral assembly and budding. **Filoviruses** released from infected cells incorporated raft-associated molecules, suggesting that viral exit occurs at the rafts. Ectopic expression of **Ebola** matrix protein and glycoprotein supported raft-dependent release of filamentous, virus-like particles (VLPs), strikingly similar to live virus as revealed by electron microscopy. Our findings also revealed that the entry of **filoviruses** requires functional rafts, identifying rafts as the site of virus attack. The identification of rafts as the gateway for the entry and exit of **filoviruses** and raft-dependent generation of VLPs have, important implications for development of therapeutics and vaccination strategies against infections with **Ebola** and **Marburg** viruses.

L19 ANSWER 11 OF 18 MEDLINE on STN
2001567679. PubMed ID: 11672925. **Marburg** virus vaccines: comparing classical and new approaches. Hevey M; Negley D; VanderZanden L; Tammariello R F; Geisbert J; Schmaljohn C; Smith J F; Jahrling P B; **Schmaljohn A L**. (Virology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 21702, USA.) Vaccine, (2001 Nov 12) Vol. 20, No. 3-4, pp. 586-93. Journal code: 8406899. ISSN: 0264-410X. Pub. country: England: United Kingdom. Language: English.

AB An effort to develop a safe and effective vaccine for **Marburg** virus (MBGV), one of the **filoviruses** known to cause high mortality rates in humans, led us to compare directly some of the merits of modern versus classical vaccine approaches for this agent. Prior work had established the MBGV-glycoprotein (GP), the only known virion surface antigen, as a candidate for inclusion in a vaccine. In this study, we vaccinated groups

MBGV-GP expressed by baculovirus recombinants, MBGV-GP delivered as a DNA vaccine, or MBGV-GP delivered via an alphavirus RNA replicon. Serological responses were evaluated, and animals were challenged with a lethal dose of MBGV given either subcutaneously or via aerosol. Killed MBGV and replicon-delivered MBGV-GP were notably immunogenic and protective against MBGV, but results did not exclude any approach and suggested a role for DNA vaccines in immunological priming.

L19 ANSWER 12 OF 18 MEDLINE on STN
2001412022. PubMed ID: 11461707. Folate receptor-alpha is a cofactor for cellular entry by **Marburg** and **Ebola** viruses. Chan S Y; Empig C J; Welte F J; Speck R F; **Schmaljohn A**; Kreisberg J F; Goldsmith M A. (Gladstone Institute of Virology and Immunology, San Francisco, CA 94141, USA.) Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 117-26. Journal code: 0413066. ISSN: 0092-8674. Pub. country: United States. Language: English.

AB Human infections by **Marburg** (MBG) and **Ebola** (EBO) viruses result in lethal hemorrhagic fever. To identify cellular entry factors employed by MBG virus, noninfectible cells transduced with an expression library were challenged with a selectable pseudotype virus packaged by MBG glycoproteins (GP). A cDNA encoding the folate receptor-alpha (FR-alpha) was recovered from cells exhibiting reconstitution of viral entry. A FR-alpha cDNA was recovered in a similar strategy employing EBO pseudotypes. FR-alpha expression in Jurkat cells facilitated MBG or EBO entry, and FR-blocking reagents inhibited infection by MBG or EBO. Finally, FR-alpha bound cells expressing MBG or EBO GP and mediated syncytia formation triggered by MBG GP. Thus, FR-alpha is a significant cofactor for cellular entry for MBG and EBO viruses.

L19 ANSWER 13 OF 18 MEDLINE on STN
2000484684. PubMed ID: 10924796. Recombinant RNA replicons derived from attenuated Venezuelan equine encephalitis virus protect guinea pigs and mice from **Ebola** hemorrhagic fever virus. Pushko P; Bray M; Ludwig G V; Parker M; **Schmaljohn A**; Sanchez A; Jahrling P B; Smith J F. (Virology Division, US Army Medical Research Institute for Infectious Diseases, Fort Detrick, Frederick, MD 21702, USA.) Vaccine, (2000 Aug 15) Vol. 19, No. 1, pp. 142-53. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB RNA replicons derived from an attenuated strain of Venezuelan equine encephalitis virus (VEE), an alphavirus, were configured as candidate vaccines for **Ebola** hemorrhagic fever. The **Ebola** nucleoprotein (NP) or glycoprotein (GP) genes were introduced into the VEE RNA downstream from the VEE 26S promoter in place of the VEE structural protein genes. The resulting recombinant replicons, expressing the NP or GP genes, were packaged into VEE replicon particles (NP-VRP and GP-VRP, respectively) using a bipartite helper system that provided the VEE structural proteins in trans and prevented the regeneration of replication-competent VEE during packaging. The immunogenicity of NP-VRP and GP-VRP and their ability to protect against lethal **Ebola** infection were evaluated in BALB/c mice and in two strains of guinea pigs. The GP-VRP alone, or in combination with NP-VRP, protected both strains of guinea pigs and BALB/c mice, while immunization with NP-VRP alone protected BALB/c mice, but neither strain of guinea pig. Passive transfer of sera from VRP-immunized animals did not confer protection against lethal challenge. However, the complete protection achieved with active immunization with VRP, as well as the unique characteristics of the VEE replicon vector, warrant further testing of the safety and efficacy of NP-VRP and GP-VRP in primates as candidate vaccines against **Ebola** hemorrhagic fever.

L19 ANSWER 14 OF 18 MEDLINE on STN
2000165041. PubMed ID: 10698744. Epitopes involved in antibody-mediated protection from **Ebola** virus. Wilson J A; Hevey M; Bakken R; Guest S; Bray M; **Schmaljohn A L**; Hart M K. (Virology Division, U.S. Army Medical Research Institute of Infectious Diseases, 1425 Porter Street, Fort Detrick, Frederick, MD 21702-5011, USA.) Science, (2000 Mar 3) Vol. 287, No. 5458, pp. 1664-6. Journal code: 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.

AB To determine the ability of antibodies to provide protection from **Ebola** viruses, monoclonal antibodies (mAbs) to the **Ebola** glycoprotein were generated and evaluated for efficacy. We identified several protective mAbs directed toward five unique epitopes on **Ebola** glycoprotein. One of the epitopes is conserved among all **Ebola** viruses that are known to be pathogenic for humans. Some protective mAbs were also effective therapeutically when administered to mice 2 days after exposure to lethal **Ebola** virus. The identification of protective mAbs has important implications for developing vaccines and therapies for **Ebola** virus.

L19 ANSWER 15 OF 18 MEDLINE on STN
1999033090. PubMed ID: 9813200. **Marburg** virus vaccines based upon alphavirus replicons protect guinea pigs and nonhuman primates. Hevey M; Negley D; Pushko P; Smith J; **Schmaljohn A**. (United States Army Medical Research Institute for Infectious Diseases, Fort Detrick, Frederick, Maryland, 21702, USA.) Virology, (1998 Nov 10) Vol. 251, No. 1, pp.

States. Language: English.

AB **Marburg** virus (MBGV), for which no vaccines or treatments currently exist, causes an acute hemorrhagic fever with a high mortality rate in humans. We previously showed that immunization with either killed MBGV or a glycoprotein (GP) subunit prevented lethal infection in guinea pigs. In the studies reported here, an RNA replicon, based upon Venezuelan equine encephalitis (VEE) virus, was used as a vaccine vector; the VEE structural genes were replaced by genes for MBGV GP, nucleoprotein (NP), VP40, VP35, VP30, or VP24. Guinea pigs were vaccinated with recombinant VEE replicons (packaged into VEE-like particles), inoculated with MBGV, and evaluated for viremia and survival. Results indicated that either GP or NP were protective antigens while VP35 afforded incomplete protection. As a more definitive test of vaccine efficacy, nonhuman primates (cynomolgus macaques) were inoculated with VEE replicons expressing MBGV GP and/or NP. Three monkeys received packaged control replicons (influenza HA); these died 9 or 10 days after challenge, with typical MBGV disease. MBGV NP afforded incomplete protection, sufficient to prevent death but not disease in two of three macaques. Three monkeys vaccinated with replicons which expressed MBGV GP, and three others vaccinated with both replicons that expressed GP or NP, remained aviremic and were completely protected from disease.

L19 ANSWER 16 OF 18 MEDLINE on STN

1998321157. PubMed ID: 9657001. DNA vaccines expressing either the GP or NP genes of **Ebola** virus protect mice from lethal challenge. Vanderzanden L; Bray M; Fuller D; Roberts T; Custer D; Spik K; Jahrling P; Huggins J; **Schmaljohn A**; Schmaljohn C. (Virology Division, United States Army Medical Research Institute of Infectious Diseases, Ft. Detrick, Maryland 21702-5011, USA.) Virology, (1998 Jun 20) Vol. 246, No. 1, pp. 134-44. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB DNA vaccines expressing the envelope glycoprotein (GP) or nucleocapsid protein (NP) genes of **Ebola** virus were evaluated in adult, immunocompetent mice. The vaccines were delivered into the skin by particle bombardment of DNA-coated gold beads with the Powderject-XR gene gun. Both vaccines elicited antibody responses as measured by ELISA and elicited cytotoxic T cell responses as measured by chromium release assays. From one to four vaccinations with 0.5 microgram of the GP DNA vaccine resulted in a dose-dependent protection from **Ebola** virus challenge. Maximal protection (78% survival) was achieved after four vaccinations. Mice were completely protected with a priming dose of 0.5 microgram of GP DNA followed by three or four subsequent vaccinations with 1.5 micrograms of DNA. Partial protection could be observed for at least 9 months after three immunizations with 0.5 microgram of the GP DNA vaccine. Comparing the GP and NP vaccines indicated that approximately the same level of protection could be achieved with either vaccine.

L19 ANSWER 17 OF 18 MEDLINE on STN

1998278390. PubMed ID: 9617828. Quantitative studies of heteropolymer-mediated binding of inactivated **Marburg** virus to the complement receptor on primate erythrocytes. Nardin A; Sutherland W M; Hevey M; **Schmaljohn A**; Taylor R P. (Department of Biochemistry, School of Medicine, University of Virginia, Charlottesville 22908, USA.) Journal of immunological methods, (1998 Feb 1) Vol. 211, No. 1-2, pp. 21-31. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Previous in vitro and in vivo experiments in our laboratory have demonstrated that cross-linked bispecific monoclonal antibody (mAb) complexes (Heteropolymers, HP) facilitate binding of prototype pathogens to primate erythrocytes (E) via the E complement receptor, CR1. These E-bound immune complexes are safely and rapidly cleared from the bloodstream. In order to generate a robust bispecific system for HP-mediated clearance of real pathogens such as **Filoviruses**, we have developed the necessary methodologies and reagents using both inactivated **Marburg** virus (iMV) and a recombinant form of its surface envelope glycoprotein (rGP). We identified mAbs which bind rGP in solution phase immunoprecipitation experiments. HP were prepared by chemically cross-linking an anti-CR1 mAb with several of these anti-**Marburg** virus mAbs and used to facilitate binding of iMV and rGP to monkey and human E. These HP mediate specific and quantitative binding (> or = 90%) of both antigens to monkey and human E. Binding was also demonstrable in an indirect RIA. E with bound **Marburg** virus were probed with 125I labeled mAbs to the **Marburg** surface glycoprotein and more than 100 mAbs are bound per E. It should be possible to adapt this general approach to other pathogens, and experiments underway should lead to an in vivo test of HP-mediated clearance of **Marburg** virus.

L19 ANSWER 18 OF 18 MEDLINE on STN

1998087840. PubMed ID: 9426460. Antigenicity and vaccine potential of **Marburg** virus glycoprotein expressed by baculovirus recombinants. Hevey M; Negley D; Geisbert J; Jahrling P; **Schmaljohn A**. (Virology Division, United States Army Medical Research Institute for Infectious Diseases,

Vol. 239, No. 1, pp. 206-16. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB There is no effective vaccine for **Marburg** virus (MBGV) or any other **filovirus**, nor enough pertinent information to expedite rational vaccine development. To ascertain some of the minimal requirements for a MBGV vaccine, we determined whether whole inactivated MBGV, or a baculovirus-expressed virion subunit, could be used to immunize guinea pigs against a lethal infection. Baculovirus recombinants were made to express the MBGV glycoprotein (GP) either as a full-length, cell-associated molecule or a slightly truncated (5.4%) product secreted into medium; the latter, for its far greater ease in manipulation, was tested for its vaccine potential. Like MBGV GP, both the full-length and truncated GP expressed by baculovirus recombinants were abundantly glycosylated with both N- and O-linked glycans; differences in glycosylation were detectable, but these could not be shown to affect antigenicity with respect to available antibodies. The recombinant truncated glycoprotein elicited protection against lethal challenge with the MBGV isolate from which it was constructed and less effectively against an antigenically disparate MBGV isolate. Killed (irradiated) MBGV antigen was protective, in a reciprocal fashion, against both MBGV types. In a preliminary assessment of possible protective mechanisms, serum antibodies from immune animals were shown to be sufficient for protecting naive guinea pigs from lethal MBGV infections

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L19          18 S L18 AND (FILOVIR? OR EBOLA OR MARBURG)

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CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)
HIGHEST GRANTED PATENT NUMBER: US7007305
HIGHEST APPLICATION PUBLICATION NUMBER: US2006048257
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ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Mar 2006 (20060302/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005


=> s (filovir? or marburg or ebola)
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1336 EBOLA
L20 2474 (FILOVIR? OR MARBURG OR EBOLA)

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820 GP2
17040 GP
620 SGP
L21 351 L20 AND (GP1 OR GP2 OR GP OR SGP)

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820 GP2
L22 17 L21 AND (GP1 AND GP2)

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L23 9 L22 AND AY<2003

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L23 ANSWER 1 OF 9 USPATFULL on STN
2004:328000 Development of a preventive vaccine for **filovirus** infection in primates.
Nabel, Gary, Washington, DC, UNITED STATES
Yang, Zhi-yong, Potomac, MD, UNITED STATES
Sullivan, Nancy, Kensington, MD, UNITED STATES
Sanchez, Anthony, Lilburn, GA, UNITED STATES
US 2004259825 A1 20041223
APPLICATION: US 2004-491121 A1 20040823 (10)
WO 2002-US30251 20020924
PRIORITY: US 2001-326476P 20011001 (60)
DOCUMENT TYPE: Utility; APPLICATION.

AB The present invention relates generally to viral vaccines and, more particularly, to **filovirus** vaccines and methods of eliciting an immune response against a **filovirus** or disease caused by infection with **filovirus**.

CLM What is claimed is:

1. A bimodal priming composition and boosting composition for priming and boosting an immune response to an antigen in an individual comprising (1) a priming composition comprised of a DNA plasmid comprising a nucleic acid molecule encoding **Ebola, Marburg,** Lassa, retrovirus, paramyxovirus, or influenza virus glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a DNA plasmid taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, and (2) a boosting composition comprised of a replication-deficient adenovirus comprising a nucleic acid molecule encoding **Ebola, Marburg,** Lassa, retrovirus, paramyxovirus, or influenza virus glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a replication-deficient adenovirus taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, for production of said antigen by expression from said DNA plasmid and replication-deficient adenovirus, whereby an immune response to the antigen previously primed in the individual is boosted.

2. A bimodal priming composition and boosting composition for priming and boosting an immune response to an antigen in an individual comprising (1) a priming composition comprised of a DNA plasmid comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a DNA plasmid taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, and (2) a boosting composition comprised of a replication-deficient adenovirus comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a replication-deficient adenovirus taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, for production of said antigen by expression from said DNA plasmid and replication-deficient adenovirus, whereby an immune response to the antigen previously primed in the individual is boosted.

3. A bimodal priming composition and boosting composition for priming and boosting an immune response to an antigen in an individual comprising (1) a priming composition comprised of a first genetic construct comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, and (2) a boosting composition comprised of a second genetic construct comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, or recombinantly produced **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or

identity thereto, wherein the first genetic construct is taken from the group consisting of plasmid DNA, replication-deficient adenovirus, replication-deficient vaccinia virus, recombinant avipox virus, and recombinant herpes virus, and wherein the second genetic construct is taken from the group consisting of replication-deficient adenovirus, replication-deficient vaccinia virus, recombinant avipox virus, and recombinant herpes virus, for production of said antigen by expression from said first genetic construct and second genetic construct, whereby an immune response to the antigen previously primed in the individual is boosted.

4. A method of boosting an immune response to an antigen in an individual comprising providing to said individual a boosting composition comprised of a replication-deficient adenovirus comprising a nucleic acid molecule encoding **Ebola, Marburg,** Lassa, retrovirus, paramyxovirus, or influenza virus glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a replication-deficient adenovirus taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, for production of said antigen by expression from said replication-deficient adenovirus, whereby an immune response to the antigen previously primed in the individual is boosted.

5. A method of boosting an immune response to an antigen in an individual comprising providing to said individual a boosting composition comprised of a replication-deficient adenovirus comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a replication-deficient adenovirus taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, for production of said antigen by expression from said replication-deficient adenovirus, whereby an immune response to the antigen previously primed in the individual is boosted.

6. A method of boosting an immune response to an antigen in an individual comprising providing to said individual a boosting composition comprised of a second genetic construct comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, or recombinantly produced **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, for production of said antigen by expression from said replication-deficient adenovirus, wherein the second genetic construct is taken from the group consisting of replication-deficient adenovirus, replication-deficient vaccinia virus, recombinant avipox virus, and recombinant herpes virus, whereby an immune response to the antigen previously primed in the individual during production of said antigen by expression from a first genetic construct is boosted, and wherein the first genetic construct is taken from the group consisting of plasmid DNA, replication-deficient adenovirus, replication-deficient vaccinia virus, recombinant avipox virus, and recombinant herpes virus.

7. A method of inducing an immune response to an antigen in an individual comprising providing to said individual a priming composition comprising of a DNA plasmid comprising a nucleic acid molecule encoding **Ebola, Marburg,** Lassa, retrovirus, paramyxovirus, or influenza virus glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a DNA plasmid taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, and then providing to said individual a boosting composition comprised of a replication-deficient adenovirus comprising a nucleic acid molecule encoding **Ebola, Marburg,** Lassa, retrovirus, paramyxovirus, or influenza virus glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a replication-deficient adenovirus taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, for production of said antigen by expression from said DNA plasmid and replication-deficient adenovirus, whereby an immune response to the antigen previously primed in the individual is boosted.

8. A method of inducing an immune response to an antigen in an individual comprising providing to said individual a priming composition comprising of a DNA plasmid comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa, glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a DNA plasmid taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, and then providing to said individual a boosting composition comprised of a replication-deficient adenovirus comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa, retrovirus glycoprotein or nucleoprotein or epitope-bearing domain thereof, or a replication-deficient adenovirus taken from Table 2 or its insert, or analog thereof having at least 95% identity thereto, for production of said antigen by expression from said DNA plasmid and

antigen previously primed in the individual is boosted.

9. A method of inducing an immune response to an antigen in an individual comprising providing to said individual a priming composition comprising of a first genetic construct comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, and then providing to said individual a boosting composition comprised of a second genetic construct comprising a nucleic acid molecule encoding **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, or recombinantly produced **Ebola, Marburg,** or Lassa glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the first genetic construct is taken from the group consisting of plasmid DNA, replication-deficient adenovirus, replication-deficient vaccinia virus, recombinant avipox virus, and recombinant herpes virus, and wherein the second genetic construct is taken from the group consisting of replication-deficient adenovirus, replication-deficient vaccinia virus, recombinant avipox virus, and recombinant herpes virus, for production of said antigen by expression from said first genetic construct and second genetic construct, whereby an immune response to the antigen previously primed in the individual is boosted.

10. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

11. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

12. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

13. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

14. A composition or method of any of claims 19 claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Marburg** glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

15. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

16. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

17. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

18. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

19. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Marburg** nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

20. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

21. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

22. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

23. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

24. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Marburg** glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

25. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

26. A composition or method of any of claims 19 claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

27. A composition or method of any of claims 1 claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

28. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston

at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

29. A composition of claim 1, wherein the DNA plasmid or first genetic construct comprises a nucleic acid molecule encoding **Marburg** nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

30. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

31. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

32. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

33. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

34. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Marburg** glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

35. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

36. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

37. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

38. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

39. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Marburg** nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto.

40. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire glycoprotein or epitope-bearing domain thereof or

glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

41. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

42. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

43. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

44. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Marburg** glycoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has an internal or carboxy deletion to delete the mucin-like domain, the furin cleavage site, the fusion peptide domain, the heptad repeat domain, the transmembrane anchor domain, or the intracellular domain.

45. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Zaire nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

46. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Sudan nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

47. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Ivory Coast nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and

carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

48. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Ebola** Reston nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

49. A composition of claim 1, wherein the replication-defective adenovirus or second genetic construct comprises a nucleic acid molecule encoding **Marburg** nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, wherein the glycoprotein has a truncation at the carboxy terminus to delete the transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the heptad repeat domain and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain, or a truncation at the carboxy terminus to delete the mucin-like domain, furin cleavage site, fusion peptide domain, heptad repeat domain, and transmembrane anchor and intracellular domain.

50. VRC6000 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6000.

51. VRC6001 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6001.

52. VRC6002 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6002.

53. VRC6003 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6003.

54. VRC6004 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6004.

55. VRC6005 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6005.

56. VRC6006 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6006.

57. VRC6007 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6007.

58. VRC6008 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6008.

59. VRC6052 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6052.

60. VRC6101 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6101.

61. VRC6110 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6110.

62. VRC6200 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6200.

63. VRC6201 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6201.

64. VRC6202 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6202.

65. VRC6300 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6300.

66. VRC6301 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6301.

67. VRC6302 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6302.

68. VRC6303 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6303.

69. VRC6310 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6310.

70. VRC6351 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6351

71. VRC6400 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6400.

72. VRC6401 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6401.

73. VRC6500 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6500.

74. VRC6600 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6600.

75. VRC6601 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6601.

76. VRC6602 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6602.

77. VRC6603 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6603.

78. VRC6604 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6604.

79. VRC6701 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6701.

80. VRC6702 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6702.

81. VRC6710 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6710.

82. VRC6800 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6800.

83. VRC6801 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6801.

84. VRC6810 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6810.

85. VRC6811 or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6811.

86. CMV/R **Ebola GP** (Z) deltaTM/h (codon optimized) or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is CMV/R **Ebola GP** (Z) deltaTM/h (codon optimized).

87. pVR1012 **Ebola GP** (Z, P87666) delta TM/h (codon optimized) or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is pVR1012 **Ebola GP** (Z, P87666) delta TM/h (codon optimized).

88. CMV/R **Ebola GP** (S/Gulu) delta TM/h (codon optimized) or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is CMV/R **Ebola GP** (S/Gulu) delta TM/h (codon optimized).

89. CMV/R **Ebola GP** (S,Q66798) delta TM/h (codon optimized) or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is CMV/R **Ebola GP** (S,Q66798) delta TM/h (codon optimized).

composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6802, pVR1012x/s Lassa (codon optimized).

91. VRC6703, pVR1012x/s **Marburg** delta TM/h (codon optimized) or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is VRC6703, pVR1012x/s **Marburg** (codon optimized).

92. CMV/R **Ebola** NP or a composition of claim 1, wherein the DNA plasmid or replication-deficient adenovirus taken from Table 2 is CMV/R **Ebola** NP.

93. A composition of claim 1, wherein the priming or boosting composition is administered intramuscularly.

94. A composition of claim 1, wherein the boosting composition is administered about 2-3 weeks, or 4 weeks, or 8 weeks, or 16 weeks, or 20 weeks, or 24 weeks, or 28 weeks, or 32 weeks after administration of the priming composition.

95. A composition of claim 1, wherein the priming or boosting composition is administered in combination with an adjuvant.

96. A composition of claim 1, wherein the priming or boosting composition is administered in combination with a cytokine or nucleic acid encoding therefor.

97. A composition of claim 1, wherein the DNA plasmid is administered at a dose of 10 micrograms to 50 milligrams/injection.

98. A composition of claim 1, wherein the replication-deficient adenovirus is administered at a dose of 5×10 7 to 1×10 12 particles/injection.

99. A composition of claim 1, wherein the priming or boosting composition is further comprised of either the same or a different DNA plasmid or replication-deficient adenovirus comprising a nucleic acid molecule encoding a second **Ebola** glycoprotein or nucleoprotein or epitope-bearing domain thereof or analog thereof having at least 95% identity thereto, and wherein the second **Ebola** glycoprotein or nucleoprotein is different from the first.

L23 ANSWER 2 OF 9 USPATFULL on STN
2004:70637 Monoclonal antibodies and complementarity-determining regions binding to **Ebola** glycoprotein.
Hart, Mary Kate, Frederick, MD, UNITED STATES
Wilson, Julie, Birmingham, AL, UNITED STATES
US 2004053865 A1 20040318
APPLICATION: US 2002-226795 A1 20020823 (10)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In this application are described **Ebola GP** monoclonal antibodies, epitopes recognized by these monoclonal antibodies, and the sequences of the variable regions of some of these antibodies. Also provided are mixtures of antibodies of the present invention, as well as methods of using individual antibodies or mixtures thereof for the detection, prevention, and/or therapeutical treatment of **Ebola** virus infections in vitro and in vivo.

CLM What is claimed is:
1. An isolated monoclonal antibody which binds **Ebola** virus **GP**, which monoclonal antibody comprises a heavy chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:11.

2. The isolated monoclonal antibody which binds **Ebola** virus **GP** of claim 1, which monoclonal antibody comprises a heavy chain variable region encoded by the DNA sequence SEQ ID NO:11.

3. An isolated monoclonal antibody which binds **Ebola** virus **GP**, which monoclonal antibody comprises a light chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:16.

4. The isolated monoclonal antibody which binds **Ebola** virus **GP** of claim 3, which monoclonal antibody comprises a light chain variable region encoded by the DNA sequence SEQ ID NO:16.

5. The isolated monoclonal antibody of claim 1, which further comprises a light chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:16.

6. The isolated monoclonal antibody of claim 2, which further comprises

7. An isolated monoclonal antibody which binds **Ebola** virus **GP**, which monoclonal antibody comprises a heavy chain variable region having a sequence that has at least 90% homology to amino acid sequence SEQ ID NO:12.

8. The isolated monoclonal antibody which binds **Ebola** virus **GP** of claim 7, which monoclonal antibody comprises a heavy chain variable region having the amino acid sequence SEQ ID NO:12.

9. An isolated monoclonal antibody which binds **Ebola** virus **GP**, which monoclonal antibody comprises a light chain variable region having a sequence that has at least 90% homology to amino acid sequence SEQ ID NO:17.

10. The isolated monoclonal antibody which binds **Ebola** virus **GP** of claim 9, which monoclonal antibody comprises a light chain variable region having the amino acid sequence SEQ ID NO:17.

11. The isolated monoclonal antibody of claim 7, which further comprises a light chain variable region having a sequence that has at least 90% homology to amino acid sequence SEQ ID NO:17.

12. The isolated monoclonal antibody of claim 8, which further comprises a light chain variable region having the amino acid sequence SEQ ID NO:17.

13. An isolated monoclonal antibody which binds **Ebola** virus **GP**, which comprises a heavy chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:13, SEQ ID NO:14, and SEQ ID NO:15.

14. The isolated monoclonal antibody of claim 13, wherein SEQ ID NO:13 is located at position 31-35, SEQ ID NO:14 is located at position 50-65, and SEQ ID NO:15 is located at position 95-102, which amino acid positions are numbered according to the Kabat system.

15. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which comprises a light chain comprising the complementarity-determining regions having the amino sequences of SEQ ID NO:18, SEQ ID NO:19, and SEQ ID NO:20.

16. The isolated monoclonal antibody of claim 15, wherein SEQ ID NO:18 is located at position 24-34, SEQ ID NO:19 is located at position 50-56, and SEQ ID NO:20 is located at position 89-97, which amino acid positions are numbered according to the Kabat system.

17. The isolated monoclonal antibody of claim 13, which further comprises a light chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:18, SEQ ID NO:19, and SEQ ID NO:20.

18. The isolated monoclonal antibody of claim 14, which further comprises a light chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:18 located at position 24-34, SEQ ID NO:19 located at position 50-56, and SEQ ID NO:20 located at position 89-97, which amino acid positions are numbered according to the Kabat system.

19. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which monoclonal antibody comprises a heavy chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:21.

20. The isolated monoclonal antibody which recognizes **Ebola** virus **GP** of claim 19, which monoclonal antibody comprises a heavy chain variable region encoded by the DNA sequence SEQ ID NO:21.

21. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which monoclonal antibody comprises a light chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:26.

22. The isolated monoclonal antibody which recognizes **Ebola** virus **GP** of claim 21, which monoclonal antibody comprises a light chain variable region encoded by the DNA sequence SEQ ID NO:26.

23. The isolated monoclonal antibody of claim 19 which further comprises a light chain variable region encoded by the DNA sequence encoded by the DNA sequence having at least 90% homology to SEQ ID NO:26.

24. The isolated monoclonal antibody of claim 20 which further comprises

25. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which monoclonal antibody comprises a heavy chain variable region having an amino acid sequence having at least 90% homology to the amino acid sequence SEQ ID NO:22.

26. The isolated monoclonal antibody which recognizes **Ebola** virus **GP** of claim 25, which monoclonal antibody comprises a heavy chain variable region having the amino acid sequence SEQ ID NO:22.

27. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which monoclonal antibody comprises a light chain variable region having an amino acid sequence having at least 90% homology to the amino acid sequence SEQ ID NO:27.

28. The isolated monoclonal antibody which recognizes **Ebola** virus **GP** of claim 27, which monoclonal antibody comprises a light chain variable region having the amino acid sequence SEQ ID NO:27.

29. The isolated monoclonal antibody of claim 25, which further comprises a light chain variable region having the amino acid sequence having at least 90% homology to the amino acid sequence SEQ ID NO:27.

30. The isolated monoclonal antibody of claim 26, which further comprises a light chain variable region having an amino acid sequence SEQ ID NO:27.

31. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which comprises a heavy chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:23, SEQ ID NO:24, and SEQ ID NO:25.

32. The isolated monoclonal antibody of claim 31, wherein SEQ ID NO:23 is located at position 31-35, SEQ ID NO:24 is located at position 50-65, and SEQ ID NO:25 is located at position 95-102, which amino acid positions are numbered according to the Kabat system.

33. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which comprises a light chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:28, SEQ ID NO:29, and SEQ ID NO:30.

34. The isolated monoclonal antibody of claim 33, wherein SEQ ID NO:28 is located at position 24-34, SEQ ID NO:29 is located at position 50-56, and SEQ ID NO:30 is located at position 89-97, which amino acid positions are numbered according to the Kabat system.

35. The isolated monoclonal antibody of claim 31 which further comprises a light chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:28, SEQ ID NO:29, and SEQ ID NO:30.

36. The isolated monoclonal antibody of claim 32 which further comprises a light chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:28 located at position 24-34, SEQ ID NO:29 located at position 50-56, and SEQ ID NO:30 located at position 89-97, which amino acid positions are numbered according to the Kabat system.

37. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which monoclonal antibody comprises a heavy chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:31.

38. The isolated monoclonal antibody which recognizes **Ebola** virus **GP** of claim 37, which monoclonal antibody comprises a heavy chain variable region encoded by the DNA sequence SEQ ID NO:31.

39. An isolated monoclonal antibody which recognizes **Ebola** virus **GP**, which monoclonal antibody comprises a light chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:36.

40. The isolated monoclonal antibody which recognizes **Ebola** virus **GP** of claim 39, which monoclonal antibody comprises a light chain variable region encoded by the DNA sequence SEQ ID NO:36.

41. The isolated monoclonal antibody of claim 37 which further comprises a light chain variable region encoded by the DNA sequence having at least 90% homology to SEQ ID NO:36.

42. The isolated monoclonal antibody of claim 38 which further comprises a light chain variable region encoded by the DNA sequence SEQ ID NO:36.

which monoclonal antibody comprises a heavy chain variable region having an amino acid sequence having at least 90% homology to SEQ ID NO:32.

44. The isolated monoclonal antibody which binds **Ebola** virus **GP** of claim 43, which monoclonal antibody comprises a heavy chain variable region having the amino acid sequence SEQ ID NO:32.

45. An isolated monoclonal antibody which binds **Ebola** virus **GP,** which monoclonal antibody comprises a light chain variable region having an amino acid sequence having at least 90% homology to SEQ ID NO:37.

46. The isolated monoclonal antibody which binds **Ebola** virus **GP** of claim 45, which monoclonal antibody comprises a light chain variable region having the amino acid sequence SEQ ID NO:37.

47. The isolated monoclonal antibody of claim 43 which further comprises a light chain variable region having an amino acid sequence having at least 90% homology to SEQ ID NO:37.

48. The isolated monoclonal antibody of claim 44 which further comprises a light chain variable region having the amino acid sequence SEQ ID NO:37.

49. An isolated monoclonal antibody which binds **Ebola** virus **GP,** which comprises a heavy chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:33, SEQ ID NO:34, and SEQ ID NO:35.

50. The isolated monoclonal antibody of claim 49, wherein SEQ ID NO:33 is located at position 31-35, SEQ ID NO:34 is located at position 50-65, and SEQ ID NO:35 is located at position 95-102, wherein the amino acid positions are numbered according to the Kabat system.

51. An isolated monoclonal antibody which binds **Ebola** virus **GP,** which comprises a light chain comprising complementarity-determining regions having the amino sequences of SEQ ID NO:38, SEQ ID NO:39, and SEQ ID NO:40.

52. The isolated monoclonal antibody of claim 51, wherein SEQ ID NO:38 is located at position 24-34, SEQ ID NO:39 is located at position 50-56, SEQ ID NO:40 is located at position 89-97, wherein the amino acid positions are numbered according to the Kabat system.

53. The isolated monoclonal antibody of claim 49 which further comprises a light chain that comprises the complementarity-determining regions having the amino sequences of SEQ ID NO:38, SEQ ID NO:39, and SEQ ID NO:40.

54. The isolated monoclonal antibody of claim 50 which further comprises a light chain that comprises the complementarity-determining regions having the amino sequences of SEQ ID NO:38 located at position 24-34, SEQ ID NO:39 located at position 50-56, and SEQ ID NO:40 located at position 89-97, wherein the amino acid positions are numbered according to the Kabat system.

55. A composition comprising the isolated **Ebola** virus monoclonal antibodies of an antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, an antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and an antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376.

56. The composition of claim 55, further comprising a pharmaceutically acceptable excipient.

57. The composition of claim 55, which contains between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376.

58. A method for preventing **Ebola** virus infection in a mammal, comprising the step of administering to a mammal, prior to the mammal being challenged with **Ebola,** an effective amount of a composition comprising the isolated **Ebola** virus monoclonal antibodies of an antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, an antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and an antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376.

59. The method of claim 58, wherein the composition further comprises a pharmaceutically acceptable excipient.

about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376.

61. A passive vaccine against **Ebola** virus infection comprising an effective amount of a composition comprising the isolated **Ebola** virus monoclonal antibodies of an antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, an antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and an antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376.

62. A method for ameliorating an **Ebola** virus infection in a mammal, comprising the step of administering to a mammal infected with **Ebola** an effective amount of a composition comprising the isolated **Ebola** virus monoclonal antibodies of an antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, an antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and an antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376.

63. The method of claim 62, wherein the composition further comprises a pharmaceutically acceptable excipient.

64. The method of claim 62, wherein the composition contains between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and between about 1.0 mg/kg and about 50 mg/kg of the antibody produced by hybridoma EGP 6D8-1-2 accession no. PTA 376.

65. A method for detecting **Ebola** virus in a sample, said method comprising: (i) incubating the sample with an effective amount of at least one monoclonal antibody selected from the group consisting of the antibody produced by hybridoma EGP 13F6-1-2 accession no. PTA 373, the antibody produced by hybridoma EGP 13C6-1-1 accession no. PTA 375; and the antibody produced by hybridoma EGP 6D8-1-2, under conditions which allow the formation of an antibody-**Ebola** virus complex; and (ii) detecting the antibody-**Ebola** virus complex wherein the presence or absence of the complex indicates the presence or absence of **Ebola** virus in the sample.

66. The method of claim 65 wherein, said monoclonal antibody is chosen from the group consisting of Mab 13F6, Mab 13C6, and Mab 6D8.

67. The method of claim 65 wherein said monoclonal antibodies compete for binding to **GP** with an antibody chosen from the group consisting of Mab 13F6, Mab 13C6, and Mab 6D8.

68. The method of claim 58 wherein said composition comprises antibodies which compete for binding to **GP** with an antibody chosen from the group consisting of Mab 13F6, Mab 13C6, and Mab 6D8.

69. The method of claim 62 wherein said composition comprises antibodies which compete for binding to **GP** with an antibody chosen from the group consisting of Mab 13F6, Mab 13C6, and Mab 6D8.

70. A kit for detecting **Ebola** virus in a biological sample, said kit comprising: (i) a container holding at least one monoclonal antibody selected from the group consisting of Mab 13F6, Mab 13C6, and Mab 6D8, and (ii) instructions for using said at least one antibody for the purpose of binding to **Ebola** virus to form an immunological complex and detecting the formation of the immunological complex such that presence or absence of immunological complex correlates with presence or absence of **Ebola** virus in said sample.

71. A kit for detecting **Ebola** virus in a biological sample, said kit comprising: (i) a container holding at least one monoclonal antibody that competes for binding to **Ebola GP** with a monoclonal antibody selected from the group consisting of Mab 13F6, Mab, 13C6, and Mab 6D8, and (ii) instructions for using said at least one antibody for the purpose of binding to **Ebola** virus to form an immunological complex and detecting the formation of the immunological complex such that presence or absence of immunological complex correlates with presence or absence of **Ebola** virus in said sample.

L23 ANSWER 3 OF 9 USPATFULL on STN
2004:38116 Composition and method for stimulating immune response to pathogen using complex adenoviral vector.
Wang, Danher, Mt. Pleasant, SC, UNITED STATES
US 2004028652 A1 20040212

DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Genetic vaccines and methods are provided for enhancing the immunity of a host such as a human to one or more pathogens. In one aspect, a method of enhancing the immunity of a host to a pathogen is provided. The method comprises administering to the host a recombinant virus comprising an antigen sequence that is heterologous to a native progenitor of the recombinant adenovirus and encodes a viral antigen from a pathogenic virus, expression of which is under the transcriptional control of a first promoter; and a cytokine sequence that is heterologous to the native progenitor of the recombinant adenovirus and encodes a cytokine, expression of which is under the transcriptional control of a second promoter. Expression of the antigen and cytokine sequences elicits an immune response directed against the viral antigen upon infection of the host by the recombinant virus. The method can be used for immunizing a host against a wide variety of pathogen viruses, such as HIV, **Ebola** virus, **Marburg** virus, hepatitis B virus, hepatitis C virus, influenza virus, human simplex virus, human papilloma virus and respiratory syncytial virus.

CLM What is claimed is:

1. A method of enhancing the immunity of a host to a pathogen, comprising: administering to the host a recombinant virus comprising an antigen sequence that is heterologous to a native progenitor of the recombinant adenovirus and encodes a viral antigen from a pathogenic virus, expression of which is under the transcriptional control of a first promoter; and a cytokine sequence that is heterologous to the native progenitor of the recombinant adenovirus and encodes a cytokine, expression of which is under the transcriptional control of a second promoter, expression of the antigen and cytokine sequences eliciting an immune response directed against the viral antigen upon infection of the host by the recombinant virus.

2. The method of claim 1, wherein the recombinant adenovirus is replication-incompetent.

3. The method of claim 1, wherein the antigen sequence and the cytokine sequence are positioned in the E1 and E3 region of the native progenitor of the recombinant adenovirus, respectively.

4. The method of claim 1, wherein the antigen sequence and the cytokine sequence are positioned in the E1 and E4 region of the native progenitor of the recombinant adenovirus, respectively.

5. The method of claim 1, wherein the antigen sequence and the cytokine sequence are positioned in the E3 and E4 region of the native progenitor of the recombinant adenovirus, respectively.

6. The method of claim 1, wherein the first promoter is a promoter homologous to the native progenitor of the recombinant adenovirus.

7. The method of claim 1, wherein the first or second promoter is a promoter heterologous to the native progenitor of the recombinant adenovirus.

8. The method of claim 1, wherein the first or second promoter is heterologous to the native progenitor of the recombinant adenovirus and is a promoter selected from the group consisting of CMV promoter, SV40 promoter, retrovirus LTR promoter, and chicken cytoplasmic β-actin promoter.

9. The method of claim 1, wherein the first and second promoters are the same promoter positioned in the same location of the recombinant adenovirus.

10. The method of claim 9, wherein the antigen and cytokine sequences are expressed bicistronically by the same promoter.

11. The method of claim 10, wherein the first and second antigen sequences are expressed bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

12. The method of claim 1, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-4, interleukin-12, β-interferon, λ-interferon, γ-interferon, granulocyte colony stimulating factor, and granulocyte-macrophage colony stimulating factor.

13. The method of claim 1, wherein the pathogenic virus is a human immunodeficiency virus.

14. The method of claim 13, wherein the viral antigen is an HIV surface, core/capsid, regulatory, enzyme or accessory protein.

15. The method of claim 13, wherein the viral antigen is selected from the group consisting of HIV gp120, gp41, Gag, p17, p24, p2, p7, p1, p6, Tat, Rev, PR, RT, IN, Vif, Vpr, Vpx, Vpu and Nef.

16. The method of claim 1, wherein the pathogenic virus is influenza virus.

17. The method of claim 16, wherein the viral antigen is a glycoprotein of the influenza virus.

18. The method of claim 16, wherein the viral antigen is influenza glycoprotein HA1, HA2 or NA.

19. The method of claim 1, wherein the pathogenic virus is **Ebola** virus.

20. The method of claim 19, wherein the viral antigen is an **Ebola** glycoprotein.

21. The method of claim 19, wherein the viral antigen is **Ebola GP1** or **GP2** protein.

22. The method of claim 19, wherein the viral antigen is an **Ebola** nucleocapsid protein.

23. The method of claim 1, wherein the pathogenic virus is **Marburg** virus.

24. The method of claim 23, wherein the viral antigen is a **Marburg** glycoprotein.

25. The method of claim 23, wherein the viral antigen is a **Marburg** nucleocapsid protein.

26. The method of claim 1, wherein the pathogenic virus is hepatitis virus.

27. The method of claim 26, wherein the hepatitis virus is hepatitis A, B, C, D or E virus.

28. The method of claim 27, wherein the viral antigen is surface antigen or core protein of hepatitis B virus.

29. The method of claim 27, wherein the viral antigen is SHBsAg, MHBsAg, or LHBsAg of hepatitis B virus.

30. The method of claim 27, wherein the viral antigen is a surface antigen or core protein of hepatitis C virus.

31. The method of claim 27, wherein the viral antigen is NS3, NS4 or NS5 antigen of hepatitis C virus.

32. The method of claim 1, wherein the pathogenic virus is respiratory syncytial virus.

33. The method of claim 32, wherein the viral antigen is a glycoprotein or a fusion protein of respiratory syncytial virus

34. The method of claim 1, wherein the pathogenic virus is herpes simplex virus.

35. The method of claim 34, wherein the pathogenic virus is herpes simplex virus type-1 or type-2.

36. The method of claim 35, wherein the viral antigen is glycoprotein D from herpes simplex virus type-2.

37. The method of claim 1, wherein the pathogenic virus is human papilloma virus.

38. The method of claim 37, wherein the viral antigen is E6 or E7 of human papilloma virus.

39. The method of claim 1, wherein the viral antigen is a full-length antigenic viral protein or a portion of the antigenic viral protein that contains the predominant antigen, neutralizing antigen, or epitope of the pathogenic virus.

40. The method of claim 1, wherein the viral antigen is a modified antigen that is mutated from a glycoprotein of the pathogenic virus such that the viral antigen is rendered non-functional as a viral component but retains its antigenicity.

antigen includes deletions in the proteolytic cleavage site of the glycoprotein, and duplications and rearrangement of immunosuppressive peptide regions of the glycoprotein.

42. The method of claim 1, wherein the native E1, E3, or E4 region of the recombinant adenovirus is deleted to such an extent that renders the recombinant adenovirus replication-incompetent.

43. The method of claim 1, wherein the native E4 region of the recombinant adenovirus except ORF6 is deleted.

44. The method of claim 1, wherein the native E1 region of the recombinant adenovirus is completely deleted, the native E3 of the recombinant adenovirus is functionally deleted, and the native E4 region of the recombinant adenovirus except ORF6 is deleted.

45. The method of claim 1, wherein the recombinant adenovirus further comprises a second antigen sequence that encodes a second viral antigen from a second pathogenic virus and is expressed bicistronically under the transcriptional control of the second promoter.

46. The method of claim 45, wherein the viral antigen and the second viral antigen are different.

47. The method of claim 45, wherein the pathogenic virus and the second pathogenic virus are the same.

48. The method of claim 45, wherein the pathogenic virus and the second pathogenic virus are of the same type but of different subtype or clade.

49. The method of claim 45, wherein the pathogenic virus and the second pathogenic virus are different types of the same virus.

50. The method of claim 45, wherein the pathogenic virus and the second pathogenic virus are different viruses.

51. The method of claim 45, wherein the pathogenic virus or the second pathogenic virus is selected from the group consisting of HIV-1, HIV-2, herpes simplex virus type 1, herpes simplex virus type 2, **Ebola** virus, **Marburg** virus, hepatitis A, B, C, D, and E viruses, respiratory syncytial virus, and human papilloma virus.

52. The method of claim 45, wherein the second antigen sequence is expressed by the second promoter bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

53. The method of claim 1, wherein administering to the host the recombinant virus is performed intramuscularly, intratracheally, subcutaneously, intranasally, intradermally, rectally, orally or parentally.

L23 ANSWER 4 OF 9 USPATFULL on STN
2003:209962 Expression of HIV polypeptides and production of virus-like particles.
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Megede, Jan zur, San Francisco, CA, United States
Greer, Catherine, Oakland, CA, United States
Selby, Mark, San Francisco, CA, United States
Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
US 6602705 B1 20030805
APPLICATION: US 1999-475515 19991230 (9)
PRIORITY: US 1998-114495P 19981231 (60)
US 1999-168471P 19991201 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the efficient expression of HIV polypeptides in a variety of cell types, including, but not limited to, mammalian, insect, and plant cells. Synthetic expression cassettes encoding the HIV Gag-containing polypeptides are described, as are uses of the expression cassettes in applications including DNA immunization, generation of packaging cell lines, and production of Env-, tat- or Gag-containing proteins. The invention provides methods of producing Virus-Like Particles (VLPs), as well as, uses of the VLPs including, but not limited to, vehicles for the presentation of antigens and stimulation of immune response in subjects to whom the VLPs are administered.
CLM What is claimed is:
1. An expression cassette, comprising a polynucleotide sequence encoding a polypeptide including an HIV Gag polypeptide, wherein the polynucleotide sequence encoding said Gag polypeptide comprises a sequence having at least 90% sequence identity to the sequence presented

2. The expression cassette of claim 1, comprising, a polynucleotide sequence encoding a polypeptide including an HIV Gag polypeptide, wherein the polynucleotide sequence encoding said Gag polypeptide comprises a sequence having at least 90% sequence identity to the sequence presented as SEQ ID NO:9.

3. The expression cassette of claim 1, wherein said polynucleotide sequence encoding a polypeptide including an HIV Gag polypeptide comprises a sequence having at least 90% sequence identity to the sequence presented as SEQ ID NO:4.

4. The expression cassette of claim 1, wherein said polynucleotide sequence further includes a polynucleotide sequence encoding an HIV protease polypeptide.

5. The expression cassette of claim 4,wherein the nucleotide sequence encoding said polypeptide comprises a sequence having at least 90% sequence identity to a sequence selected from the group consisting of: SEQ ID NO:5, SEQ ID NO:78, and SEQ ID NO:79.

6. The expression cassette of claim 1, wherein said polynucleotide sequence further includes a polynucleotide sequence encoding an HIV reverse transcriptase polypeptide.

7. The expression cassette of claim 6, wherein the nucleotide sequence encoding said polypeptide comprises a sequence having at least 90% sequence identity to a sequence selected from the group consisting of: SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, and SEQ ID NO:84.

8. The expression cassette of claim 1, wherein said polynucleotide sequence further includes a polynucleotide sequence encoding an HIV tat polypeptide.

9. The expression cassette of claim 8, wherein the nucleotide sequence encoding said polypeptide comprises a sequence having at least 90% sequence identity to a sequence selected from the group consisting of: SEQ ID NO:87, SEQ ID NO:88, and SEQ ID NO:89.

10. The expression cassette of claim 1,wherein said polynucleotide sequence further includes a polynucleotide sequence encoding an HIV polymerase polypeptide, wherein the nucleotide sequence encoding said polypeptide comprises a sequence having at least 90% sequence identity to the sequence presented as SEQ ID NO:6.

11. The expression cassette of claim 1, wherein said polynucleotide sequence further includes a polynucleotide sequence encoding an HIV polymerase polypeptide, wherein (i) the nucleotide sequence encoding said polypeptide comprises a sequence having at least 90% sequence identity to the sequence presented as SEQ ID NO:4, and (ii) wherein the sequence is modified by deletions of coding regions corresponding to reverse transcriptase and integrase.

12. The expression cassette of claim 11, wherein said polynucleotide sequence preserves T-helper cell and CTL epitopes.

13. The expression cassette of claim 1, wherein said polynucleotide sequence further includes a polynucleotide sequence encoding an HCV core polypeptide, wherein the nucleotide sequence encoding said polypeptide comprises a sequence having at least 90% sequence identity to the sequence presented as SEQ ID NO:7.

14. A recombinant expression system for use in a selected host cell, comprising, an expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the selected host cell.

15. The recombinant expression system of claim 14, wherein said control elements are selected from the group consisting of a transcription promoter, a transcription enhancer element, a transcription termination signal, polyadenylation sequences, sequences for optimization-of initiation of translation, and translation termination sequences.

16. The recombinant expression system of claim 15, wherein said transcription promoter is selected from the group consisting of CMV, CMV+intron A, SV40, RSV, HIV-Ltr, MMLV-ltr, and metallothionein.

17. A cell comprising an expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the selected cell.

19. The cell of claim 18, wherein the cell is selected from the group consisting of BHK, VERO, HT1080, 293, RD, COS-7, and CHO cells.

20. The cell of claim 19, wherein said cell is a CHO cell.

21. The cell of claim 17, wherein the cell is an insect cell.

22. The cell of claim 21, wherein the cell is either Trichoplusia ni (Tn5) or Sf9 insect cells.

23. The cell of claim 17, wherein the cell is a bacterial cell.

24. The cell of claim 17, wherein the cell is a yeast cell.

25. The cell of claim 17, wherein the cell is a plant cell.

26. The cell of claim 17, wherein the cell is an antigen presenting cell.

27. The cell of claim 26, wherein the antigen-presenting cell is a lymphoid cell selected from the group consisting of macrophage, monocytes, dendritic cells, B-cells, T-cells, stem cells, and progenitor cells thereof.

28. The cell of claim 17, wherein the cell is a primary cell.

29. The cell of claim 17, wherein the cell is an immortalized cell.

30. The cell of claim 17, wherein the cell is a tumor-derived cell.

31. A cell line useful for packaging lentivirus vectors, comprising suitable host cells that have been transfected with an expression vector containing an expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the host cell.

32. A cell line useful for packaging lentivirus vectors, comprising suitable host cells that have been transfected with an expression vector containing an expression cassette of claim 2, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the host cell.

33. A cell line useful for packaging lentivirus vectors, comprising suitable host cells that have been transfected with an expression vector containing an expression cassette of claim 3, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the host cell.

34. A cell line useful for packaging lentivirus vectors, comprising suitable host cells that have been transfected with an expression vector containing an expression cassette of claim 11, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the host cell.

35. A gene delivery vector for use in a Mammalian subject, comprising a suitable gene delivery vector for use in said subject, wherein the vector comprises an expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the subject.

36. A gene delivery vector comprising an alphavirus vector construct, wherein said alphavirus construct comprises an expression cassette according to claim 1.

37. The gene delivery vector of claim 36, wherein the alphavirus vector construct is a cDNA vector construct.

38. The gene delivery vector of claim 36, wherein the alphavirus comprises a recombinant alphavirus particle preparation.

39. The gene delivery vector of claim 36, wherein the vector comprises a eukaryotic layered vector initiation system.

L23 ANSWER 5 OF 9 USPATFULL on STN
2003:181681 End-locked five-helix protein.
Zhou, Genfa, Chestnut Hill, MA, UNITED STATES
US 2003125515 A1 20030703
APPLICATION: US 2002-193412 A1 20020711 (10)
PRIORITY: US 2001-304152P 20010711 (60)
DOCUMENT TYPE: Utility; APPLICATION.

AB End-locked five-helix protein, which is made up of three N-helices and two C-helices of HIV gp41, four inside linkers, and at least one terminal linker; the helices are connected by the inside linkers, and the terminal linker is connected to an helix and is capable of cross-linking with one of the inside linkers, is disclosed.

CLM What is claimed is:

1. An end-locked five-helix protein comprising: three N-helices and two C-helices of HIV gp41 four inside linkers, and at least one terminal linker; wherein the helices are connected by the inside linkers, and the terminal linker is connected to an helix and is capable of cross-linking with one of the inside linkers.

2. The protein according to claim 1 comprising from N-terminus to C-terminus: an N-terminal linker, a first N-helix, a first inside linker, a first C-helix, a second inside linker, a second N-helix, a third inside linker, a second C-helix, a fourth inside linker, a third N-helix, and a C-terminal linker; wherein the N-terminal linker cross-links with the second inside linker or the fourth inside linker, and the C-terminal linker cross-links with the first inside linker or the third inside linker.

3. The protein according to claim 2 wherein both the inside linkers and terminal linkers comprise amino acid residues.

4. The protein according to claim 3 wherein terminal linkers cross-link with the inside linkers through the interaction of side chains of amino acid residues.

5. The protein according to claim 4 wherein the terminal linkers cross-link with the inside linker through covalent bond.

6. The protein according to claim 5 wherein the covalent bond is a disulfide bond.

7. An isolated protein having a sequence selected from the group consisting of: SEQ ID NO.: 1 SEQ ID NO.: 2 SEQ ID NO.: 3 and SEQ ID NO.: 4.

8. An isolated polynucleotide encoding the protein according to claim 7.

9. The protein according to claim 1 comprising from N-terminus to C-terminus: a first N-helix, a first inside linker, a first C-helix, a second inside linker, a second N-helix, a third inside linker, a second C-helix, a fourth inside linker, a third N-helix, and C-terminal linker; wherein the C-terminal linker cross-links with the first inside linker or the third inside linker.

10. The protein according to claim 1 comprising from N-terminus to C-terminus: an N-terminal linker, a first N-helix, a first inside linker, a first C-helix, a second inside linker, a second N-helix, a third inside linker, a second C-helix, and a fourth inside linker, a third N-helix; wherein the N-terminal linker cross-links with the second inside linker or the fourth inside linker.

11. A method of inhibiting the entry of HIV into a cell, the method comprising contacting HIV with the protein according to claim 1.

12. The method according to claim 11, wherein the cell is a human cell.

13. A method of inhibiting HIV infection in a host, the method comprising administering to the host a composition comprising the protein according to claim 1.

14. The method according to claim 13, wherein the host is human.

15. A method of eliciting an immune response to HIV in a host, the method comprising introducing into the host a composition comprising the protein according to claim 1.

16. A method of identifying a compound that inhibits HIV infection, the method comprising contacting the protein according to claim 1 with the compound.

17. The method according to claim 16 further comprising determining whether the compound inhibits HIV infection of mammalian cells.

L23 ANSWER 6 OF 9 USPATFULL on STN

2003:158947 Chimeric **filovirus** glycoprotein.

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APPLICATION: US 2002-66506 A1 20020131 (10)
PRIORITY: US 2001-267522P 20010131 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Chimeric **GP** molecules were constructed which contain portions of both the EBOV and MBGV **GP** proteins by swapping the subunits between EBOV and MBGV. The chimeric molecules were cloned into an alphavirus replicon which offers the advantage of high protein expression levels in mammalian cells and is a proven vaccine vector. These chimeric molecules fully protected guinea pigs from MBGV challenge, and conversely protected the animals from EBOV challenge. These results indicate that a protective epitope resides within the **GP2** subunit of the MBGV **GP** protein and at least partially within the **GP2** subunit of the EBOV **GP** protein. Additionally these results show that a construction of a single-component bivalent vaccine protective in guinea pigs is achievable.

CLM What is claimed is:

1. A chimeric **filovirus GP** protein comprising **GP1** and **GP2** wherein said **GP1** is chosen from a **filovirus** different than that of **GP2**.

2. The chimeric **filovirus GP** protein according to claim 1 wherein said **GP1** or **GP2** is from a **filovirus** chosen from the Genera consisting of **Ebola** and **Marburg**.

3. The chimeric **filovirus GP** protein according to claim 2 wherein said **Ebola** is chosen from the species Zaire, Sudan, Reston, and Cote d'Ivoire.

4. The chimeric **filovirus GP** protein according to claim 2 wherein said **Marburg** is chosen from the species Musoke, Ravn, and Popp.

5. The chimeric **filovirus GP** protein according to claim 1 wherein said **GP1** is from **Ebola** and **GP2** is from **Marburg**.

6. The chimeric **filovirus GP** protein according to claim 5 wherein said **Ebola** is strain Zaire and said **Marburg** is strain Musoke.

7. The chimeric **filovirus GP** protein according to claim 1 wherein said **GP1** is from **Marburg** and **GP2** is from **Ebola**.

8. The chimeric **filovirus GP** protein according to claim 7 wherein said **Marburg** is strain Musoke and said **Ebola** is strain Zaire.

9. The chimeric **filovirus GP** protein according to claim 1 wherein said **GP1** is from **Marburg** strain Musoke and said **GP2** is from **Marburg** strain Ravn.

10. The chimeric **filovirus GP** protein according to claim 1 wherein said **GP1** is from **Marburg** strain Ravn and said **GP2** is from **Marburg** strain Musoke.

11. The chimeric **filovirus GP** protein according to claim 6 wherein said chimeric **GP** is EBGP1/MBGP2 identified in SEQ ID NO:2 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

12. A DNA fragment encoding the chimeric protein of claim 11, said DNA identified in SEQ ID NO:1 and conservative substitutions thereof.

13. The chimeric **filovirus GP** protein according to claim 8 wherein said chimeric **GP** is MBGP1/EBGP2 identified in SEQ ID NO:4 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

14. A DNA fragment encoding the chimeric protein of claim 13, said DNA identified in SEQ ID NO:3.

15. The chimeric **filovirus GP** protein according to claim 9 wherein said chimeric **GP** is MUSGP1/RVNGP2 identified in SEQ ID NO:6 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

16. A DNA fragment encoding the chimeric protein of claim 15, said DNA identified in SEQ ID NO:5.

17. The chimeric **filovirus GP** protein according to claim 10 wherein said chimeric **GP** is RVNGP1/MUSGP2 identified in SEQ ID NO:8 and conservative substitutions thereof, or an immunologically identifiable portion thereof.

18. A DNA fragment encoding the chimeric protein of claim 17, said DNA identified in SEQ ID NO:7.

19. A recombinant DNA construct comprising: (i) a vector, and (ii) a DNA fragment encoding a chimeric **filovirus GP** protein according to claim 1.

20. The recombinant DNA construct according to claim 19 wherein said DNA fragment encodes any of the following chimeric proteins chosen from the group consisting of: (i) **Marburg** Musoke **GP1/Ebola** Zaire **GP2** (ii) **Ebola** Zaire **GP1**/Marbug Musoke **GP2** (iii) **Marburg** Musoke **GP1/Marburg** Ravn **GP2** (iv) **Marburg** Ravn **GP1/Marburg** Musoke **GP2**

21. A recombinant DNA construct according to claim 20 wherein said vector is an expression vector.

22. A recombinant DNA construct according to claim 20 wherein said vector is a prokaryotic vector.

23. A recombinant DNA construct according to claim 20 wherein said vector is a eukaryotic vector.

24. A recombinant DNA construct according to claim 20 wherein said vector is a VEE virus replicon vector.

25. The recombinant DNA construct according to claim 24 wherein said construct is EBOV-MAY SP1 (aa1-501)/MBGV-MUS **GP2** (aa436-681).

26. The recombinant DNA construct according to claim 24 wherein said construct is MBGV-MUD **GP1** (aa1-435)/EBOV-MAY **GP2** (aa502-676).

27. The recombinant DNA construct according to claim 24 wherein said construct is MBGV-RVN **GP1** (aa1-435)/MBGV-MUS **GP2** (aa436-681).

28. The recombinant DNA construct according to claim 24 wherein said construct is MBGV-MUS **GP1** (aa1-435)/MBGV-RVN **GP2** (aa436-681).

29. Self replicating RNA produced from the construct of any of claims 24-28.

30. Infectious alphavirus particles produced from packaging the self replicating RNA of claim 29.

31. A pharmaceutical composition comprising infectious alphavirus particles according to claim 30 in an effective immunogenic amount in a pharmaceutically acceptable carrier and/or adjuvant.

32. A host cell transformed with a recombinant DNA construct according to claim 19.

33. A host cell according to claim 32 wherein said host cell is prokaryotic.

34. A host cell according to claim 32 wherein said host cell is eukaryotic.

35. A method for producing chimeric **filovirus GP** proteins comprising culturing the cells according to claim 33 under conditions such that said DNA fragment is expressed and said chimeric protein is produced.

36. A method for producing chimeric **filovirus GP** proteins comprising culturing the cells according to claim 34 under conditions such that said DNA fragment is expressed and said chimeric protein is produced.

37. A vaccine for more than one **filovirus** comprising viral particles containing one or more replicon RNA encoding chimeric **GP** from one or more **filovirus**.

38. A vaccine against **Ebola** Zaire virus infection and **Marburg** Musoke virus infection comprising a chimeric **GP** protein according to claim 5.

39. A vaccine against **Ebola** Zaire virus infection and **Marburg** Musoke virus infection comprising a chimeric **GP** protein according to claim 7.

40. A vaccine against **Marburg** Musoke virus infection and **Marburg** Ravn virus infection comprising a chimeric **GP** protein according to claim 9.

41. A vaccine against **Marburg** Musoke virus infection and **Marburg** Ravn virus infection comprising a chimeric **GP** protein according to claim 10.

42. A vaccine against **Ebola** Zaire virus infection and **Marburg** Musoke virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 25.

43. A vaccine against **Ebola** Zaire virus infection and **Marburg** Musoke virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 26.

44. A vaccine against **Marburg** Musoke virus infection and **Marburg** Ravn virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 27.

45. A vaccine against **Marburg** Musoke virus infection and **Marburg** Ravn virus infection comprising infectious alphavirus particles produced from replicating RNA produced from the construct of claim 28.

46. A pharmaceutical composition comprising a chimeric peptide encoded by any of SEQ ID NO:1, 3, 5, or 7 in a pharmaceutically acceptable amount, in a pharmaceutically acceptable carrier and/or adjuvant.

47. A bivalent **filovirus** vaccine antigen comprising a chimeric **GP** protein comprising **GP1** or a portion thereof from a first **filovirus** and **GP2** or a portion thereof from a second **filovirus**, said antigen able to elicit an immune response to two **filoviruses** in a subject.

48. A multivalent **filovirus** vaccine antigen comprising a chimeric **GP** protein wherein **GP1** and **GP2** are comprised of portions of **GP1** and **GP2** chosen from different **filoviruses**, said antigen able to elicit an immunt response to more than two **filoviruses** in a subject.

L23 ANSWER 7 OF 9 USPATFULL on STN
2003:95971 Adenovirus vector with multiple expression cassettes.
Wang, Danher, Mt. Pleasant, SC, United States
GenPhar, Inc., Mt. Pleasant, SC, United States (U.S. corporation)
US 6544780 B1 20030408
APPLICATION: US 2000-585599 20000602 (9)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Genetic vaccines and methods are provided for enhancing the immunity of a host such as a human to one or more pathogens. In one embodiment, a recombinant benign virus is provided as the genetic vaccine. The recombinant virus comprises: an antigen sequence heterologous to the recombinant virus that encodes a viral antigen from a pathogenic virus, expression of the viral antigen eliciting an immune response directed against the viral antigen and cells expressing the viral antigen in a host upon infection of the host by the recombinant virus; and an immuno-stimulator sequence heterologous to the recombinant virus that encodes an immuno-stimulator whose expression in the host enhances the immunogenicity of the viral antigen. The recombinant virus is replication-incompetent and does not causes a malignancy naturally associated with the pathogenic virus in the host. The genetic vaccines can be used for immunizing a host against a wide variety of pathogens, such as HIV, **Ebola** virus, hepatitis B virus, hepatitis C virus, influenza virus, pathogenic bacteria and parasites.

CLM What is claimed is:
1. A recombinant adenovirus comprising: in an E1, E3 or E4 region of the adenovirus, an antigen sequence that is heterologous to a native progenitor of the recombinant adenovirus and encodes a first viral antigen from a first pathogenic virus and a second viral antigen from a second pathogenic virus, the first and second viral antigens being expressed bicistronically under transcriptional control of a first promoter located in the same region as the antigen sequence; and in an E4, E3 or E1 region of the adenovirus that does not comprise the antigen sequence, an immuno-stimulator sequence that is heterologous to the native progenitor of the recombinant virus and encodes a first immuno-stimulator, the immuno-stimulator being expressed under transcriptional control of a second promoter located in the same region as the immuno-stimulator sequence, wherein a portion of or the whole native E1, E3 or E4 region is deleted to such an extent that renders the recombinant adenovirus replication-incompetent.

2. The recombinant adenovirus of claim 1, wherein the heterologous antigen sequence and the immuno-stimulator sequence are positioned in the E1 and E3 region of the native progenitor of the recombinant adenovirus, respectively.

3. The recombinant adenovirus of claim 1, wherein the heterologous antigen sequence or the immuno-stimulator sequence is positioned in the E4 region of the native progenitor of the recombinant adenovirus.

4. The recombinant adenovirus of claim 1, wherein the first promoter is a promoter homologous to the native progenitor of the recombinant adenovirus.

5. The recombinant adenovirus of claim 1, wherein the first promoter or

the recombinant virus.

6. The recombinant adenovirus of claim 5, wherein the promoter heterologous to a native progenitor of the recombinant virus is a promoter selected from the group consisting of CMV promoter, SV40 promoter, retrovirus LTR- promoter, and chicken cytoplasmic β-actin promoter.

7. The recombinant adenovirus of claim 1, wherein the first or second pathogenic virus is a human immunodeficiency virus.

8. The recombinant adenovirus of claim 7, wherein the first or second viral antigen is an HIV glycoprotein or capsid protein.

9. The recombinant adenovirus of claim 7, wherein the first or second viral antigen is selected from the group consisting of HIV-GP120, GP41, P24, Tat, Vif, and Rev protein.

10. The recombinant adenovirus of claim 1, wherein the first or second pathogenic virus is influenza virus.

11. The recombinant adenovirus of claim 10, wherein the first or second viral antigen is a glycoprotein of the influenza virus.

12. The recombinant adenovirus of claim 11, wherein the first or second viral antigen is influenza glycoprotein HA1, HA2 or NA.

13. The recombinant adenovirus of claim 1, wherein the first or second pathogenic virus is **Ebola** virus.

14. The recombinant adenovirus of claim 13, wherein the first or second viral antigen is an **Ebola** glycoprotein.

15. The recombinant adenovirus of claim 14, wherein the first or second viral antigen is **Ebola GP1** or **GP2** protein.

16. The recombinant adenovirus of claim 1, wherein the first or second pathogenic virus is hepatitis virus.

17. The recombinant adenovirus of claim 16, wherein the hepatitis virus is hepatitis A, B, C, D or E virus.

18. The recombinant adenovirus of claim 16, wherein the first or second viral antigen is surface antigen or core protein of hepatitis B virus.

19. The recombinant adenovirus of claim 18, wherein the first or second viral antigen is SHBsAg, MHBsAg, or LHBsAg of hepatitis B virus.

20. The recombinant adenovirus of claim 16, wherein the first or second viral antigen is a surface antigen or core protein of hepatitis C virus.

21. The recombinant adenovirus of claim 20, wherein the first or second viral antigen is NS3, NS4 or NS5 antigen of hepatitis C virus.

22. The recombinant adenovirus of claim 1, wherein the first or second pathogenic virus is respiratory syncytial virus.

23. The recombinant adenovirus of claim 22, wherein the hepatitis virus is hepatitis A, B, C, D or E virus. viral antigen is a glycoprotein or a fusion protein of respiratory syncytial virus.

24. The recombinant adenovirus of claim 1, wherein the first or second pathogenic virus is herpes simplex virus.

25. The recombinant adenovirus of claim 24, wherein the first or second pathogenic virus is herpes simplex virus type-1 or type-2.

26. The recombinant adenovirus of claim 24, wherein the first or second viral antigen is glycoprotein D from herpes simplex virus type-2.

27. The recombinant adenovirus of claim 1, wherein the first or second pathogenic virus is human papilloma virus.

28. The recombinant adenovirus of claim 27, wherein the first or second viral antigen is E6 or E7 of human papilloma virus.

29. The recombinant adenovirus of claim 1, wherein the first immuno-stimulator is a cytokine.

30. The recombinant adenovirus of claim 29, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-4, interleukin-12, β-interferon, λ-interferon,

granulocyte-macrophage colony stimulating factor.

31. The recombinant adenovirus of claim 1, wherein the first or second viral antigen is a full-length antigenic viral protein or a portion of the antigenic viral protein that contains the dominant antigen, neutralizing antigen, or epitope of the first or second pathogenic virus.

32. The recombinant adenovirus of claim 1, wherein the first or second viral antigen is a modified antigen that is mutated from a glycoprotein of the first or second pathogenic virus such that the first or second viral antigen is rendered non-functional as a viral component but retains its antigenicity.

33. The recombinant adenovirus of claim 32, wherein the modification of first or second viral antigen includes deletions in the proteolytic cleavage site of the glycoprotein, duplications or rearrangement of immunosuppressive peptide regions or the neutralizing epitope of the glycoprotein of the same or different strain or subtype of the first or second pathogenic virus.

34. The recombinant adenovirus of claim 1, wherein the second viral antigen is expressed by the first promoter bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

35. The recombinant adenovirus of claim 1, wherein the immuno-stimulator sequence further encodes a second immuno-stimulator that is expressed bicistronically by the second promoter.

36. The recombinant adenovirus of claim 35, wherein the second immuno-stimulator is expressed by the second promoter bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

37. The recombinant adenovirus of claim 35, wherein the second immuno-stimulator is the same as the first immuno-stimulator.

38. The recombinant adenovirus of claim 35, wherein the second immuno-stimulator is different from the first immuno-stimulator.

39. The recombinant adenovirus of claim 1, wherein the first viral antigen is the same as the second viral antigen.

40. The recombinant adenovirus of claim 1, wherein the first viral antigen is different from the second viral antigen.

41. The recombinant adenovirus of claim 1, wherein the native E4 region except ORF6 is deleted.

42. The recombinant adenovirus of claim 1, wherein the native E1 and E3 regions are completely deleted, and the native E4 region except ORF6 is deleted.

L23 ANSWER 8 OF 9 USPATFULL on STN
2003:50858 Recombinant influenza viruses for vaccines and gene therapy.
Kawaoka, Yoshihiro, Middleton, WI, UNITED STATES
Neumann, Gabriele, Nanuet, NY, UNITED STATES
US 2003035814 A1 20030220
APPLICATION: US 2001-971372 A1 20011004 (9)
PRIORITY: US 1999-127912P 19990406 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides a composition useful to prepare influenza A viruses, e.g., in the absence of helper virus.

CLM What is claimed is:
1. A composition comprising a plurality of orthomyxovirus vectors, comprising a) at least two vectors selected from a vector comprising a promoter operably linked to an influenza virus PA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus PB1 cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus PB2 cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus HA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus NP cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus NA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus M cDNA linked to a transcription termination sequence, and a vector comprising a promoter operably linked

sequence; and b) at least two vectors selected from a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB2, and a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NP.

2. A composition comprising a plurality of orthomyxovirus vectors, comprising a) at least two vectors selected from a vector comprising a promoter operably linked to an influenza virus PA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus PB1 cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus PB2 cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus HA cDNA linked to a transcription termination sequence, a vector comprising promoter operably linked to an influenza virus NP cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus NA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus M cDNA linked to a transcription termination sequence, and a vector comprising a promoter operably linked to an influenza virus NS cDNA linked to a transcription termination sequence; and b) at least two vectors selected from a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB2, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NP, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus HA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M2, and a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NS2.

3. A composition comprising a plurality of orthomyxovirus vectors, comprising a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PA cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PB1 cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PB2 cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus HA cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus NP cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus NA cDNA linked to a RNA polymerase I transcription termination-sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus M cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus NS cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB2, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NP, and a vector comprising a RNA polymerase I promoter linked to 5' non-coding influenza virus sequences linked to a cDNA of interest or a fragment thereof in antisense orientation linked to 3' non-coding influenza virus sequences linked to a RNA polymerase I transcription termination sequence.

4. A composition comprising a plurality of orthomyxovirus vectors, comprising a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PA cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PB1 cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PB2 cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus HA cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus NP cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus NA CDNA

vector comprising a RNA polymerase I promoter operably linked to an influenza virus M cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus NS cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB2, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NP, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus HA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M2, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NS2, and a vector comprising a RNA polymerase I promoter linked to 5' non-coding influenza virus sequences linked to a cDNA of interest or fragment thereof in antisense orientation linked to 3' non-coding influenza virus sequences linked to a RNA polymerase I transcription termination sequence.

5. The composition of claim 1 or 2 wherein the vectors of a) are linked.

6. The composition of claim 1 or 2 wherein the vectors of b) are linked.

7. The composition of claim 1 or 2 wherein each vector of a) is on a separate plasmid.

8. The composition of claim 1 or 2 wherein each vector of b) is on a separate plasmid.

9. The composition of claim 1 or 2 wherein the promoter of the vectors of a) comprise a RNA polymerase I promoter, RNA polymerase II promoter, RNA polymerase III promoter, T7 promoter, or T3 promoter.

10. The composition of claim 9 wherein the RNA polymerase I promoter is a human RNA polymerase I promoter.

11. The composition of claim 1 or 2 wherein the each of the vectors of b) further comprise a RNA transcription termination sequence.

12. The composition of claim 1 or 2 wherein the transcription termination sequence of the vectors of a) comprise a RNA polymerase I transcription termination sequence, RNA polymerase II transcription termination sequence, RNA polymerase III transcription termination sequence, or a ribozyme.

13. The composition of claim 1 or 2 further comprising a vector comprising a promoter linked to 5' non-coding influenza virus sequences linked to cDNA linked to 3' non-coding influenza virus sequences linked to a transcription termination sequence.

14. The composition of claim 1, 2, 3 or 4 wherein any one of the cDNAs is in the sense orientation.

15. The composition of claim 1, 2, 3 or 4 wherein any one of the cDNAs is in the antisense orientation.

16. A method to prepare influenza virus, comprising: contacting a cell with the composition of claim 1, 2, 3 or 4 in an amount effective to yield infectious influenza virus.

17. The method of claim 16 further comprising isolating the virus.

18. Virus obtained by the method of claim 16.

19. A composition comprising a plurality of orthomyxovirus vectors, comprising a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PA cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PB1 cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus PB2 cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a RNA polymerase I promoter operably linked to an influenza virus NP cDNA linked to a RNA polymerase I transcription termination sequence, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB2, a vector comprising a promoter operably linked to a

operably linked to a DNA segment encoding influenza virus HA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M2, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NS2, and a vector comprising a RNA polymerase I promoter linked to 5' non-coding influenza virus sequences linked to an antisense cDNA linked to 3' non-coding influenza virus sequences linked to a RNA polymerase I transcription termination sequence.

20. A method to prepare a gene delivery vehicle, comprising: contacting cells with the composition of claim 19 in an amount effective to yield influenza virus, and isolating the virus.

21. Virus obtained by the method of claim 20.

22. A cell contacted with the composition of claim 1, 2, 3, 4, or 19.

23. A cell infected with the virus of claim 18.

24. A cell infected with the virus of claim 21.

25. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus PA cDNA linked to a RNA polymerase I transcription termination sequence.

26. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus PB1 cDNA linked to a RNA polymerase I transcription termination sequence.

27. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus PB2 cDNA linked to a RNA polymerase I transcription termination sequence.

28. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus NP cDNA linked to a RNA polymerase I transcription termination sequence.

29. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus HA cDNA linked to a RNA polymerase I transcription termination sequence.

30. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus NA cDNA linked to a RNA polymerase I transcription termination sequence.

31. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus M1 cDNA linked to a RNA polymerase I transcription termination sequence.

32. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus M2 cDNA linked to a RNA polymerase I transcription termination sequence.

33. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus NS2 cDNA linked to a RNA polymerase I transcription termination sequence.

34. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus M cDNA linked to a RNA polymerase I transcription termination sequence.

35. A vector comprising a human RNA polymerase I promoter operably linked to an influenza virus NS cDNA linked to a RNA polymerase I transcription termination sequence.

36. A host cell, the genome of which is stably augmented with at least one of the following: a recombinant DNA molecule comprising a promoter finctional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second loxP site linked to an influenza virus HA coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NA coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment-comprising a transcription stop sequence linked to a second lox site linked to an influenza virus M1 coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NS2

functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus M2 coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus PA coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus PB1 coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus PB2 coding region; or a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NP coding region.

37. The host cell of claim 36 which is augmented with a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus HA coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NA coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus M1 coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NS2 coding region; and a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus M2 coding region.

38. The host cell of claim 36 wherein the cell is augmented with a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NS2 coding region.

39. The host cell of claim 36, 37 or 38 wherein the lox sites are loxP sites.

40. A method to prepare infectious replication defective influenza virus, comprising: i) contacting the host cell of claim 36 or 37 with a recombinant influenza virus comprising: vRNA comprising a Cre open reading frame, and vRNA comprising influenza genes not present in the genome of the host cell; and ii) recovering virus from the host cell.

41. A method to prepare infectious replication defective influenza virus, comprising: i) contacting the host cell of claim 38 with a recombinant influenza virus comprising: vRNA comprising a Cre open reading frame, vRNA comprising PA, vRNA comprising PB1, vRNA comprising PB2, vRNA comprising NP, vRNA comprising HA, vRNA comprising NA, vRNA comprising M1, and vRNA comprising M2; and ii) recovering virus from the host cell.

42. A method to prepare infectious replication defective influenza virus, comprising: i) contacting the host cell of claim 38 with a recombinant influenza virus comprising: vRNA comprising a Cre open reading frame, vRNA comprising PA, vRNA comprising PB1, vRNA comprising PB2, vRNA comprising NP, vRNA comprising HA, vRNA comprising NA, and vRNA comprising M; and ii) recovering virus from the host cell.

43. A method to prepare infectious replication defective virus, comprising: i) contacting the host cell of claim 36 or 37 with a vector comprising a promoter functional in the host cell operably linked to a DNA segment encoding Cre, and a plurality of vectors each comprising a promoter operably linked to an influenza gene not expressed by the host cell; and ii) recovering virus from the host cell.

44. Virus prepared by the method of claim 41.

45. A cell infected with the virus of claim 44.

46. Virus prepared by the method of claim 42.

47. A cell infected with the virus of claim 46.

48. Virus prepared by the method of claim 43.

49. A cell infected with the virus of claim 48.

50. Virus prepared by the method of claim 40.

51. A cell infected with the virus of claim 50.

52. The method of claim 40 wherein the recombinant virus further comprises vRNA comprising a desired open reading frame.

53. The method of claim 43 wherein the plurality of vectors further comprises a vector comprising a promoter linked to the 5' non-coding region of influenza virus linked to a desired open reading frame linked to the 3' non-coding region of influenza virus.

54. The method of claim 41 or 42 wherein the recombinant virus further comprises vRNA comprising a desired open reading frame.

55. A host cell, the genome of which is augmented with a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to a host cell surface binding protein coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to a fusion protein coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus M1 coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NS2 coding region; and a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus M2 coding region.

56. The host cell of claim 56 wherein the host cell surface binding protein is HA.

57. The host cell of claim 56 wherein the fusion protein is NA.

58. The host cell of claim 56 wherein the lox sites are loxP sites.

59. A host cell, the genome of which is augmented with a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to a host cell surface binding and fusion protein coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second loxP site linked to an influenza virus M1 coding region; a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first lox site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus NS2 coding region; and a recombinant DNA molecule comprising a promoter functional in the host cell linked to a first loxP site linked to a DNA segment comprising a transcription stop sequence linked to a second lox site linked to an influenza virus M2 coding region.

60. The host cell of claim 59 wherein the lox sites are loxP sites.

61. A method to prepare infectious replication defective virus, comprising: i) contacting the host cell of claim 55 or 59 with a recombinant influenza virus comprising: vRNA comprising a Cre open reading frame, vRNA comprising PA, vRNA comprising NP, vRNA comprising PB1, and vRNA comprising PB2; and ii) recovering virus from the host cell.

62. Virus prepared by the method of claim 61.

63. A cell infected with the virus of claim 62.

64. The method of claim 61 wherein the recombinant virus further comprises vRNA comprising a desired open reading frame.

65. The composition of claim 3, 4 or 19 wherein the antisense cDNA comprising the open reading frame encodes an immunogenic polypeptide or peptide of a pathogen.

66. A method to prepare influenza virus, comprising: contacting a cell with the composition of claim 65 in an amount effective to yield infectious influenza virus.

67. The method of claim 66 further comprising isolating the virus.

68. Virus obtained by the method of claim 67.

69. The method of claim 52, 53 or 64 wherein the open reading frame encodes an immunogenic polypeptide or peptide of a pathogen.

70. Virus obtained by the method of claim 69.

71. The method of claim 54 wherein the open reading frame encodes an immunogenic polypeptide or peptide of a pathogen.

72. Virus obtained by the method of claim 71.

73. A method to immunize an individual against a pathogen, comprising administering to the individual an amount of the virus of claim 68, 70 or 72 effective to immunize the individual.

74. A vector comprising a RNA polymerase I promoter operably linked to a positive sense RNA virus cDNA linked to a RNA polymerase I transcription termination sequence.

75. The vector of claim 74 wherein the cDNA is in sense orientation.

76. The vector of claim 74 wherein the cDNA is in antisense oritentation.

77. A composition comprising a vector comprising a RNA polymerase I promoter operably linked to a positive sense RNA virus cDNA in sense orientation linked to a RNA polymerase I transcription termination sequence; and a vector comprising a RNA polymerase I promoter operably linked to a positive sense RNA virus cDNA in antisense oritentation linked to a RNA polymerase I transcription termination sequence

78. A method to prepare infectious virus comprising contacting a host cell with the vector of claim 74 so as to yield infectious virus.

79. A method to prepare infectious virus comprising contacting a host cell with the composition of claim 77 so as to yield infectious virus.

80. A method to prepare influenza virus, comprising contacting a cell with a vector comprising a promoter operably linked to an influenza virus PA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus PB1 cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus PB2 cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus HA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus NP cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus NA cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to an influenza virus M cDNA linked to a transcription termination sequence, and a vector comprising a promoter operably linked to an influenza virus NS cDNA linked to a transcription termination sequence, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus PB2, and a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NP, so as to yield infectious virus.

81. The method of claim 80 further comprising a vector comprising a promoter operably linked to a DNA segment encoding influenza virus HA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NA, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M1, a vector comprising a promoter operably linked to a DNA segment encoding influenza virus M2, and a vector comprising a promoter operably linked to a DNA segment encoding influenza virus NS2.

82. The method of claim 80 or 81 further comprising a vector comprising a promoter linked to 5' non-coding influenza virus sequences linked to a cDNA of interest or a fragment thereof in antisense orientation linked to 3' non-coding influenza virus sequences linked to a transcription termination sequence.

isolating the virus.

84. Virus obtained by the method of claim 83.

85. A cell contacted with the virus of claim 84.

86. A cell infected with the virus of claim 84.

87. A method to immunize an individual against a pathogen, comprising administering to the individual an amount of the virus of claim 84 effective to immunize the individual.

88. A vector comprising a promoter operably linked to a cDNA comprising at least a portion of the genome of a negative strand RNA virus linked to a transcription termination sequence.

89. The vector of claim 88 wherein the cDNA is a portion of a nonsegmented single strand RNA virus.

90. The vector of claim 88 wherein the cDNA is obtained from a segmented single strand RNA virus.

91. The vector of claim 88 wherein the promoter is a RNA polymerase I promoter.

92. The vector of claim 88 wherein the termination sequence is a RNA polymerase I transcription termination sequence.

93. A composition comprising a plurality of viral vectors comprising a) at least one vector comprising a promoter operably linked to a cDNA comprising at least a portion of the genome of a negative strand RNA virus linked to a transcription termination sequence; and b) at least one vector comprising a promoter operably linked to a DNA segment encoding at least one viral protein of the negative strand RNA virus.

94. The composition of claim 93 wherein the promoter of the vector of a) is a RNA polymerase I promoter.

95. The composition of claim 93 wherein the vector of a) further comprises a transcription termination sequence.

96. The composition of claim 95 wherein the transcription termination sequence is a RNA polymerase I transcription termination sequence.

97. A method of preparing virus comprising contacting a host cell with the compostion of claim 88 so as to yield infectious virus.

98. A method of preparing virus comprising contacting a host cell with the vector of claim 93 so as to yield infectious virus.

99. Virus isolated by the method of any one of claims 97 or 98.

100. Use of the virus of any one of claims 18, 21, 44, 46, 48, 50, 62, 68, 70, 72, 84, or 99.

L23 ANSWER 9 OF 9 USPATFULL on STN
2002:279696 Genetic vaccine against human immunodeficiency virus.
Wang, Danher, Mt. Pleasant, SC, UNITED STATES
US 2002155127 A1 20021024
APPLICATION: US 2001-3035 A1 20011101 (10)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Recombinant adenovirus and methods of administration to a host are provided for eliciting immune response of the host to human immunodeficiency virus (HIV). The recombinant adenovirus is capable of expressing multiple wild type or mutant HIV antigens such as HIV envelope proteins without the cleavage site or the cytosolic domain, structural proteins such as Gag and its proteolytical fragments in a natural, secreted or membrane-bound form, and regulatory proteins such as Tat, Rev and Nef. Immuno-stimulators such as cytokines can also be expressed by the recombinant adenovirus to further enhance the immunogenicity of the HIV antigens.

CLM What is claimed is:
1. A recombinant adenovirus comprising: an HIV sequence encoding an HIV antigen, expression of the HIV antigen by the recombinant adenovirus eliciting an immune response directed against the HIV antigen in a host upon infection of the host by the recombinant adenovirus.

2. The recombinant adenovirus of claim 1, wherein the recombinant adenovirus is replication-incompetent.

antigen of HIV-1 or HIV-2.

4. The recombinant adenovirus of claim 1, wherein the HIV antigen is an antigen of HIV strain BH10 or pNL4-3.

5. The recombinant adenovirus of claim 1, wherein the HIV antigen is an antigen of HIV clade A, B, C, D, E, F, or G.

6. The recombinant adenovirus of claim 1, wherein the HIV antigen is an HIV glycoprotein or surface antigen.

7. The recombinant adenovirus of claim 6, wherein the HIV glycoprotein is an HIV envelope protein.

8. The recombinant adenovirus of claim 7, wherein the HIV envelope protein is a wild type or mutant gp160, gp120, or gp41.

9. The recombinant adenovirus of claim 7, wherein the cleavage site of the HIV envelope protein is inactivated by mutation.

10. The recombinant adenovirus of claim 7, wherein the C-terminal cytosolic domain of the HIV envelope protein is deleted.

11. The recombinant adenovirus of claim 7, wherein both the cleavage site and the C-terminal cytosolic domain of the HIV envelope protein are deleted.

12. The recombinant adenovirus of claim 7, wherein the HIV envelop protein is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 14, 16, 20, 21, 22, 23, and 24.

13. The recombinant adenovirus of claim 7, wherein the HIV sequence further encodes an HIV regulatory protein selected from the group consisting of Tat, Vif, Nef, and Rev.

14. The recombinant adenovirus of claim 7, wherein the HIV antigen is a modified HIV envelope protein that includes multiclade variable loops.

15. The recombinant adenovirus of claim 14, wherein the multiclade variable loops are V3 loops from at least two HIV clades.

16. The recombinant adenovirus of claim 15, wherein the at least two HIV clades are selected from the group consisting of clade A, B, C, D, E, F, and G of group M of HIV-1 isolates.

17. The recombinant adenovirus of claim 15, wherein the V3 loops are encoded by polynucleotides selected from the group consisting of SEQ ID NOs: 25, 26, 27, 28, 29, 30, and 31.

18. The recombinant adenovirus of claim 14, wherein the modified HIV envelope protein that includes multiclade variable loops is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 32, 52, and 54.

19. The recombinant adenovirus of claim 1, further comprising: a polynucleotide encoding a signal peptide that facilitates the secretion of the HIV antigen by a cell infected by the recombinant adenoviruse.

20. The recombinant adenovirus of claim 19, wherein the signal peptide is an HIV gp120 signal peptide.

21. The recombinant adenovirus of claim 19, wherein the signal peptide is encoded by SEQ ID NO: 74.

22. The recombinant adenovirus of claim 1, further comprising: a polynucleotide encoding an membrane-anchoring domain that renders the HIV antigen bound to the surface of a cell infected by the recombinant adenoviruse.

23. The recombinant adenovirus of claim 22, wherein the membrane-anchoring domain is an HIV gp41 transmembrane domain.

24. The recombinant adenovirus of claim 22, wherein the membrane-anchoring domain is encoded by SEQ ID NO: 75.

25. The recombinant adenovirus of claim 1, wherein the HIV antigen is an HIV structural protein.

26. The recombinant adenovirus of claim 25, wherein the HIV structural protein is a wild type HIV Gag.

27. The recombinant adenovirus of claim 25, wherein the HIV structural

28. The recombinant adenovirus of claim 27, wherein the proteolytic fragment of HIV Gag is selected from the group consisting of p17/24, p17 and p24.

29. The recombinant adenovirus of claim 27, wherein the proteolytic fragment of HIV Gag is in a natural, secreted or membrane bound form.

30. The recombinant adenovirus of claim 27, wherein the proteolytic fragment of Gag is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 34, 35, 36, 40, 41, 42, 46, 47, and 48.

31. The recombinant adenovirus of claim 1, further comprising: a polynucleotide encoding an HIV protease.

32. The recombinant adenovirus of claim 31, wherein the polynucleotide encoding an HIV protease is SEQ ID NO: 56.

33. The recombinant adenovirus of claim 31, wherein the HIV antigen is HIV Gag.

34. The recombinant adenovirus of claim 33, wherein the protease is expressed as a fusion protein with the HIV Gag.

35. The recombinant adenovirus of claim 33, wherein the protease is expressed separately from a promoter different from that for the HIV Gag.

36. The recombinant adenovirus of claim 33, wherein the protease is expressed as a separate protein from the same promoter for the HIV Gag via an IRES or splicing donor/acceptor mechanism.

37. The recombinant adenovirus of claim 1, further comprising: an immuno-stimulator sequence heterologous to adenovirus and encoding an immuno-stimulator whose expression in the host enhances the immunogenicity of the HIV antigen.

38. The recombinant adenovirus of claim 37, wherein the HIV sequence is positioned in the E1 region of the adenovirus and the immuno-stimulator sequence is positioned in the E4 region of the adenovirus.

39. The recombinant adenovirus of claim 37, wherein both the HIV sequence and the immuno-stimulator sequence are positioned in the E1 or E4 region of the adenovirus, and are expressed from the same promoter bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

40. The recombinant adenovirus of claim 37, wherein the expression of the HIV antigen or the immuno-stimulator is controlled by an adenoviral promoter.

41. The recombinant adenovirus of claim 37, wherein the expression of the HIV antigen or the immuno-stimulator is controlled by a non-adenoviral promoter.

42. The recombinant adenovirus of claim 41, wherein the non-adenoviral promoter is selected from the group consisting of CMV promoter, SV40 promoter, retrovirus LTR promoter, and chicken cytoplasmic β-actin promoter.

43. The recombinant adenovirus of claim 37, wherein the immuno-stimulator is a cytokine.

44. The recombinant adenovirus of claim 43, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-4, interleukin-12, β-interferon, λ-interferon, γ-interferon, granulocyte colony stimulating factor, and granulocyte-macrophage colony stimulating factor.

45. The recombinant adenovirus of claim 37, wherein the immuno-stimulator is a combination of different cytokines.

46. The recombinant adenovirus of claim 45, wherein the combination of cytokines are expressed from the same promoter but as separate proteins via an IRES mechanism or a retroviral splicing donor/acceptor mechanism.

47. A recombinant adenovirus comprising: a first HIV sequence encoding a first HIV antigen, expression of which is under the transcriptional control of a first promoter; and a second HIV sequence encoding a second HIV antigen, expression of which is under the transcriptional control of a second promoter positioned in a different region than the

eliciting an immune response directed against the first and second HIV antigens upon infection of the host by the recombinant virus.

48. The recombinant adenovirus of claim 47, wherein the recombinant adenovirus is replication-incompetent.

49. The recombinant adenovirus of claim 47, wherein the first and second HIV antigens are the same.

50. The recombinant adenovirus of claim 47, wherein the first and second HIV antigens are different.

51. The recombinant adenovirus of claim 47, wherein the first or second HIV antigen is an HIV envelope protein.

52. The recombinant adenovirus of claim 51, wherein the HIV envelope protein is a wild type or mutant gp160, gp120, or gp41.

53. The recombinant adenovirus of claim 52, wherein the cleavage site of the HIV envelope protein is inactivated by mutation.

54. The recombinant adenovirus of claim 52, wherein the C-terminal cytosolic domain of the HIV envelope protein is deleted.

55. The recombinant adenovirus of claim 52, wherein both the cleavage site and the C-terminal cytosolic domain of the HIV envelope protein are deleted.

56. The recombinant adenovirus of claim 51, wherein the first or second HIV sequence further encodes an HIV regulatory protein selected from the group consisting of Tat, Vif, Nef, and Rev.

57. The recombinant adenovirus of claim 47, wherein the first or second HIV antigen is a modified HIV envelope protein that includes multiclade variable loops.

58. The recombinant adenovirus of claim 57, wherein the multiclade variable loops are V3 loops from at least two HIV clades.

59. The recombinant adenovirus of claim 58, wherein the at least two HIV clades are selected from the group consisting of clade A, B, C, D, E, F, and G of group M of HIV-1 isolates.

60. The recombinant adenovirus of claim 58, wherein the V3 loops are encoded by polynucleotides selected from the group consisting of SEQ ID NOs: 25, 26, 27, 28, 29, 30, and 31.

61. The recombinant adenovirus of claim 47, further comprising: a polynucleotide encoding a signal peptide that facilitates the secretion of the first or second HIV antigen by a cell infected by the recombinant adenoviruse.

62. The recombinant adenovirus of claim 61, wherein the signal peptide is an HIV gp120 signal peptide.

63. The recombinant adenovirus of claim 61, wherein the signal peptide is encoded by SEQ ID NO: 74.

64. The recombinant adenovirus of claim 47, further comprising: a polynucleotide encoding an membrane-anchoring domain that renders the first or second HIV antigen bound to the surface of a cell infected by the recombinant adenoviruse.

65. The recombinant adenovirus of claim 64, wherein the membrane-anchoring domain is an HIV gp41 transmembrane domain.

66. The recombinant adenovirus of claim 64, wherein the membrane-anchoring domain is encoded by SEQ ID NO: 75.

67. The recombinant adenovirus of claim 47, wherein the first and second HIV antigen is an HIV structural protein.

68. The recombinant adenovirus of claim 67, wherein the HIV structural protein is a wild type HIV Gag.

69. The recombinant adenovirus of claim 67, wherein the HIV structural protein is a proteolytic fragment of HIV Gag.

70. The recombinant adenovirus of claim 67, wherein the proteolytic fragment of HIV Gag is selected from the group consisting of p17/24, p17 and p24.

fragment of HIV Gag is in a natural, secreted or membrane bound form.

72. The recombinant adenovirus of claim 67, wherein the proteolytic fragment of Gag is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 34, 35, 36, 40, 41, 42, 46, 47, and 48.

73. The recombinant adenovirus of claim 67, further comprising: a polynucleotide encoding an HIV protease.

74. The recombinant adenovirus of claim 73, wherein the polynucleotide encoding an HIV protease is SEQ ID NO: 56.

75. The recombinant adenovirus of claim 47, wherein the first HIV antigen is a wildtype or mutant HIV envelope protein, and the second HIV antigen is a wildtype or mutant HIV structural protein.

76. The recombinant adenovirus of claim 75, wherein wildtype or mutant HIV structural protein is wildtype Gag or a proteolytic fragment of Gag.

77. The recombinant adenovirus of claim 47, wherein both the first and second HIV antigen are a wildtype or mutant HIV envelope protein.

78. The recombinant adenovirus of claim 47, wherein both the first and second HIV antigen are a wildtype or mutant HIV structural protein.

79. The recombinant adenovirus of claim 47, further comprising: an immuno-stimulator sequence heterologous to adenovirus and encoding an immuno-stimulator whose expression in the host enhances the immunogenicity of the first or second HIV antigen.

80. The recombinant adenovirus of claim 79, wherein the first or second HIV sequence and the immuno-stimulator sequence are expressed from the same promoter bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

81. The recombinant adenovirus of claim 79, wherein the immuno-stimulator is a cytokine.

82. The recombinant adenovirus of claim 81, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-4, interleukin-12, β-interferon, λ-interferon, γ-interferon, granulocyte colony stimulating factor, and granulocyte-macrophage colony stimulating factor.

83. The recombinant adenovirus of claim 47, wherein the first or second promoter is an adenoviral promoter.

84. The recombinant adenovirus of claim 47, wherein the first or second promoter is non-adenoviral promoter.

85. The recombinant adenovirus of claim 84, wherein the non-adenoviral promoter is selected from the group consisting of CMV promoter, SV40 promoter, retrovirus LTR promoter, and chicken cytoplasmic β-actin promoter.

86. The recombinant adenovirus of claim 47, wherein the first promoter is in the E1 region of the adenovirus and the second promoter is positioned in the E4 region of the adenovirus.

87. A method for enhancing the immunity of a host to HIV infection, comprising: administering to the host a recombinant adenovirus comprising an HIV sequence encoding an HIV antigen, expression of the HIV antigen by the recombinant adenovirus eliciting an immune response directed against the HIV antigen in a host upon infection of the host by the recombinant adenovirus.

88. The method of claim 87, wherein administering to the host a recombinant adenovirus is performed intramuscularly, intratracheally, subcutaneously, intranasally, intradermally, rectally, orally or parentally.

89. The method of claim 87, wherein the recombinant adenovirus further comprises one or more immuno-stimulator sequences heterologous to adenovirus that encodes an immuno-stimulator whose expression in the host enhances the immunogenicity of the HIV antigen.

90. The method of claim 87, further comprising: administering to the host an immuno-stimulator.

91. The method of claim 90, wherein the immuno-stimulator is a cytokine selected from the group consisting of interleukin-2, interleukin-4,

γ-interferon, granulocyte colony stimulating factor, and granulocyte-macrophage colony stimulating factor.

92. A method of enhancing the immunity of a host to HIV infection, comprising: administering to the host a recombinant adenovirus comprising a first HIV sequence encoding a first HIV antigen, expression of which is under the transcriptional control of a first promoter; and a second HIV sequence encoding a second HIV antigen, expression of which is under the transcriptional control of a second promoter positioned in a different region than the first promoter, expression of the first and second HIV sequences eliciting an immune response directed against the first and second HIV antigens upon infection of the host by the recombinant virus.

93. The method of claim 92, further comprising: administering to the host the recombinant adenovirus at least once again after the initial administration of the recombinant adenovirus.

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=> d his

     (FILE 'HOME' ENTERED AT 10:36:34 ON 06 MAR 2006)

     FILE 'USPATFULL' ENTERED AT 10:36:47 ON 06 MAR 2006
                E GROGAN C C/IN
L1            1 S E4
                E HEVEY M C/IN
L2            3 S E6
L3            2 S L2 NOT L1
                E SCHMALJOHN A L/IN
L4           12 S E4-E5
L5            9 S L4 AND (FILOVIR? OR MARBURG OR EBOLA)
L6            8 S L5 NOT L1
L7            6 S L6 NOT L2

     FILE 'WPIDS' ENTERED AT 10:39:55 ON 06 MAR 2006
                E GROGAN C C/IN
L8            1 S E3
                E HEVEY M C/IN
L9            2 S E3
L10           1 S L9 NOT L8
                E SCHMALJOHN A L/IN
L11           9 S E2 OR E3
L12           8 S L11 NOT L8
L13           7 S L12 NOT L9
L14           5 S L13 AND (FILOVIR? OR MARBURG OR EBOLA)

     FILE 'MEDLINE' ENTERED AT 10:41:26 ON 06 MAR 2006
                E GROGAN C C/AU
L15           7 S E1 OR E3
                E HEVEY M C/AU
L16          10 S E2-5
L17           0 S L15 AND (FILOVIR? OR EBOLA OR MARBURG)
                E SCHMALJOHN A L/AU
L18          42 S E2-E5
L19          18 S L18 AND (FILOVIR? OR EBOLA OR MARBURG)

     FILE 'USPATFULL' ENTERED AT 10:44:43 ON 06 MAR 2006
L20        2474 S (FILOVIR? OR MARBURG OR EBOLA)
L21         351 S L20 AND (GP1 OR GP2 OR GP OR SGP)
L22          17 S L21 AND (GP1 AND GP2)
L23           9 S L22 AND AY<2003

=> file wpids
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        34.15     114.51

FILE 'WPIDS' ENTERED AT 10:47:28 ON 06 MAR 2006
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MOST RECENT DERWENT UPDATE:     200615        <200615/DW>
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http://www.stn-international.de/stndatabases/details/ipc_reform.html  and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

=> s (filovir? or marburg or ebola)
           141 FILOVIR?
           115 MARBURG
           282 EBOLA
L24        394 (FILOVIR? OR MARBURG OR EBOLA)

=> s l24 and (GP1 or GP2 or sGP or GP)
           124 GP1
            70 GP2
            62 SGP
        262064 GP
L25         29 L24 AND (GP1 OR GP2 OR SGP OR GP)

=> s l25 and (GP?/clm or ebola/clm or marburg/clm)
'CLM' IS NOT A VALID FIELD CODE
             0 GP?/CLM
             0 EBOLA/CLM
             0 MARBURG/CLM
L26          0 L25 AND (GP?/CLM OR EBOLA/CLM OR MARBURG/CLM)

=> s l25 and py<2003


SEARCH ENDED BY USER

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SEARCH ENDED BY USER

=> d l25,bib,ab,1-29

L25  ANSWER 1 OF 29  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN   2006-145780 [15]   WPIDS
DNC  C2006-049358
TI   New chimeric protein comprising a sequence of HA1 subunit of influenza
     virus hemagglutinin (HA) protein, useful for preparing a vaccine, or a
     medicament for treating an HIV-infected individual.
DC   B04 D16
IN   COPELAND, K M; DANIELS, R S; ELLIOT, A J
PA   (MEDI-N) MEDICAL RES COUNCIL
CYC  111
PI   WO 2006013367   A2 20060209 (200615)* EN   78
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            KE LS LT LU LV MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ
            UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
            DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
            KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI
            NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT
            TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT  WO 2006013367 A2 WO 2005-GB3053 20050802
PRAI US 2004-598674P      20040804; GB 2004-17390        20040804
AB   WO2006013367 A UPAB: 20060302
     NOVELTY - A chimeric protein comprising a sequence of HA1 subunit of
     influenza virus hemagglutinin (HA) protein, is new.
          DETAILED DESCRIPTION - The chimeric protein comprises:
          (A) an amino acid sequence of the HA1 subunit of influenza virus HA
     protein comprising cysteine residues at positions 30, 68 and 293 as
     numbered from the N-terminal amino acid of the HA1 subunit from influenza
     virus X31, or corresponding positions;
          (B) an amino acid sequence of the HA2 subunit of influenza virus HA
     protein comprising cysteine residues at positions 153, 160 and 164 as
     numbered from the N-terminal amino acid of the HA2 subunit from influenza
```

(C) an amino acid sequence of a heterologous protein positioned between the cysteine residues at positions 68 and 293 of (a); and having a disulphide bond between the cysteine residues at position 30 of HA1 and position 153 of HA2, at positions 68 and 293 of HA1, and at positions 160 and 164 of HA2, where the chimeric protein has the structural properties of the native HA protein such that the structure and function of the native heterologous protein are retained.

INDEPENDENT CLAIMS are also included for:

(1) a nucleic acid encoding the chimeric protein;

(2) an expression vector comprising the nucleic acid;

(3) a host cell comprising the nucleic acid;

(4) a method of producing a host cell comprising contacting a susceptible cell with the nucleic acid or the expression vector under conditions allowing uptake of the nucleic acid or expression vector into the cell;

(5) a method of producing the chimeric protein comprising culturing the host cell under conditions allowing expression of the encoded chimeric protein and optionally recovering the chimeric protein from the host cell culture;

(6) a method of producing a recombinant virus capable of expressing the chimeric protein comprising contacting a susceptible cell with the expression vector, and optionally recovering the virus from the cell;

(7) a virus obtained by the method;

(8) a target cell infected with the virus;

(9) a vaccine comprising the virus; and

(10) a composition comprising the virus and/or the chimeric protein.

ACTIVITY - Virucide; Anti-HIV. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The chimeric protein and/or the virus are useful in preparing a vaccine, or a medicament for treating an HIV-infected individual (claimed).

ADVANTAGE - Use of influenza HA in the chimeric protein allows the expression of a protein with a stable structure and the function of the native protein. In particular, the disulphide bond between the HA1 subunit (at cysteine 30) and HA2 subunit (at cysteine 153) has a stabilizing effect.

Dwg.0/7

L25 ANSWER 2 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

Full Text

AN 2006-125820 [13] WPIDS

DNC C2006-044057

TI New polypeptide useful as an antiviral or antibacterial vaccine, comprises antigenic, oligomerization, and transmembrane domains, and is capable of forming oligomers on the surface of a membrane.

DC B04 D16

IN CAPECCHI, B; MASIGNANI, V; RAPPUOLI, R; SCARSELLI, M

PA (CHIR) CHIRON SRL

CYC 111

PI WO 2006011060 A2 20060202 (200613)* EN 54

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU LV MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

ADT WO 2006011060 A2 WO 2005-IB2528 20050722

PRAI US 2004-590648P 20040723

AB WO2006011060 A UPAB: 20060224

NOVELTY - A polypeptide comprising (i) an antigenic domain, (ii) an oligomerization domain, and (iii) a transmembrane domain, where domains (i)-(iii) are not all found together in the same polypeptide in nature, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a nucleic acid encoding the polypeptide;

(2) an oligomeric protein comprising oligomerized polypeptides;

(3) a host cell expressing the polypeptide described above on its surface;

(4) a membrane preparation derived from the host cell;

(5) a pharmaceutical composition comprising the polypeptide, nucleic acid, protein, host cell, or membrane preparation above; and

(6) raising an immune response in a mammal by administering an amount of the composition to the mammal.

ACTIVITY - Antibacterial; Virucide.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The polypeptide, composition, and method are useful for raising an immune response.

ADVANTAGE - The antigenic polypeptides are expressed in oligomeric form, preferably on the surface of a membrane, which can improve their

Dwg.0/18

L25 ANSWER 3 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2005-810964 [82] WPIDS
DNC C2005-249413
TI New antiviral compounds for treatment of e.g. HIV-1 and hepatitis comprise binding element for binding viral target, first group for covalently reacting with viral target functionality and group that dissociates after bonding of first group.
DC B04 B05 D16
IN BOUSQUET-GAGNON, N; BRIDON, D P
PA (CONJ-N) CONJUCHEM INC; (HUAN-I) HUANG X; (QURA-I) QURAISHI O
CYC 110
PI WO 2005108418 A1 20051117 (200582)* EN 46
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT WO 2005108418 A1 WO 2005-CA689 20050506
PRAI US 2004-569219P 20040506
AB WO2005108418 A UPAB: 20060227
NOVELTY - Antiviral compounds that modulate the activity of virus targets and comprise a binding element for recognizing and binding a viral target, a first group for covalently reacting with functionality of the viral target, and a group optionally containing a pharmaceutical moiety that dissociates after bonding of the first group, are new.

DETAILED DESCRIPTION - Antiviral compounds that modulate the activity of virus targets, of formulae B'-R1-R2-M (I) and B'-R2-R1-M (Ia), are new.

B' = a binding element for recognizing and binding a viral target;

R1 = a first group of atoms for reacting with a functionality of the viral target so as to form a covalent bond with the target;

R2 = a second group of atoms, such that the formation of the covalent bond between R1 and the target generates cleavage of the bond between R1 and R2 so as to free R2-M;

M = H or a pharmaceutical moiety.

ACTIVITY - Virucide; Ant-HIV; Antiinflammatory; Hepatotropic. A compound of formula Ac-Trp Met Glu Trp Lys(HN-C(=O)-(CH2)6-NH-C(=O)-(CH2)3-C(=O)-O-(4-F-Ph)) Arg Glu Ile Asn Tyr Thr Ser Leu Ile His Ser Leu Ile Glu Glu Ser Gln Asn Gln Gln Glu Arg Asn Glu Gln Glu Leu Leu (a) was tested in vitro for antiviral activity against HIV-1 strain IIIB. The assay was performed in a 96-well plate with 500000 PHA-stimulated cord blood mononuclear cells (CBNC) per well, in an RPMI 1640 containing fetal bovine serum (10%), penicillin (100 U/ml), streptomycin (100 `mg/ml), glutamine (2 mM), hydrocortisone (5 mu g/ml) and interleukin-2 (20 U/ml). The cells were incubated with different concentrations of (a) for 30 - 60 minutes at 37 deg. C, prior to addition of the virus (multiplicity of infection (MOI) - 0.1 - 1), plated and grown for 7 days. The results (cpm) were obtained by reverse transcriptase. (a) (25 nM) showed RT (cpm) of 5909.

MECHANISM OF ACTION - Virus fusion and entry inhibitor.

USE - In the manufacture of a medicament for treatment of virus infections such as; HIV-1 and 2, respiratory syncytical virus (RSV), influenza virus, human Papilloma virus (HPV), **Ebola**, dengue, rubella, Epstein Barr, hepatitis, HTLV-1 and 2, Semliki Forest virus (SFV), Measles virus (MeV), yellow fever, Japanese encephalitis, West Nile or tick-borne encephalitis (TBE) virus (claimed).

ADVANTAGE - The antiviral compounds modulate the activity of viral targets including a virus, a viral antigen expressed on the surface of an infected cell, a ligand specific to a virus or viral antigen of a surface receptor on an infected cell, an infected cell, surface receptor, a peptide, an infected cell or its membrane, a viral protein expressed at the surface of an infected cell, or their fragments or specific regions (preferably **gp**-41 or a virus). The binding element has binding affinity for a region of viral target involved in activity of membrane fusion of virus infection. The subsequent covalent bonding of the first group to the region of the target results in the interruption or reduction of the activity of the target, and inhibition of the virus fusion and infections, by inhibiting the virus entry into the cell. Thus provides improved antiviral activity, as compared to the prior art compounds that bind reversibly and non-covalently to the viral targets, and thus result in dissociation from the target, enzymatic degradation and plasma clearance through kidneys, and can cause decline on their anti-viral activities due to emergence of viral resistance and/or fluctuations in, the in vivo concentrations of the drugs. Thus act as potent antifusiogenic antiviral compounds.
Dwg.0/5

L25 ANSWER 4 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

AN 2005-809991 [82] WPIDS
CR 2003-441461 [41]
DNC C2005-249028
TI New **filovirus** virus-like particle (VLP) comprising **filovirus** envelope glycoprotein (**GP**) and **filovirus** matrix protein (VP40), useful in preparing a vaccine against **Ebola** or **Marburg** virus infection.
DC B04 D16
IN AMAN, M J; BAVARI, S; SCHMALJOHN, A L; SWENSON, D; WARFIELD, K L
PA (AMAN-I) AMAN M J; (BAVA-I) BAVARI S; (SCHM-I) SCHMALJOHN A L; (SWEN-I) SWENSON D; (WARF-I) WARFIELD K L
CYC 1
PI US 2005266023 A1 20051201 (200582)* 45
ADT US 2005266023 A1 Provisional US 2001-338936P 20011107, CIP of US 2002-289839 20021107, Provisional US 2004-562800P 20040413, Provisional US 2004-562801P 20040413, US 2005-105031 20050413
PRAI US 2005-105031 20050413; US 2001-338936P 20011107;
US 2002-289839 20021107; US 2004-562800P 20040413;
US 2004-562801P 20040413
AB US2005266023 A UPAB: 20051222
NOVELTY - A new **filovirus** virus-like particle (VLP) comprising **filovirus** envelope glycoprotein (**GP**) and **filovirus** matrix protein, VP40 is produced by expressing in a cell a polynucleotide encoding **filovirus** envelope **GP** and VP40 so that the polynucleotide is expressed and the VLP is produced.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) inhibiting the association of a **filovirus** envelope **GP** with lipid rafts;

(2) preventing **filovirus** trafficking into and out of a cell which comprises disrupting lipid rafts of the cell;

(3) preventing **filovirus** trafficking;

(4) a **filovirus** vaccine comprising the VLP and a nucleic acid encoding an agent capable of eliciting an immune response against the **filovirus**;

(5) introducing an agent into a cell;

(6) an **Ebola** VLP-producing cell comprising a mammalian cell expressing **Ebola GP** and VP40;

(7) testing an agent involved in **filovirus** budding;

(8) inhibiting **Ebola** virus infection in a cell;

(9) detecting **Ebola** virus infection;

(10) a kit for detecting **Ebola** or **Marburg** virus infection comprising **Ebola** or **Marburg** VLPs;

(11) detecting **Marburg** virus infection;

(12) a kit for testing agents involved in **Ebola** budding the kit comprising a cell producing **Ebola** VLPs and ancillary reagents for detecting VLPs in the supernatant of the cells when cells are cultured;

(13) a **Marburg** VLP-producing cell comprising a mammalian cell expressing **Marburg GP** and VP40;

(14) a kit for testing agents involved in **Marburg** budding the kit comprising a cell producing **Marburg** VLPs and ancillary reagents for detecting VLPs in the supernatant of the cells when cells are cultured;

(15) an immunogenic composition comprising, in a physiologically acceptable vehicle, **Ebola** or **Marburg** VLPs;

(16) stimulating an **Ebola** virus specific immune response;

(17) stimulating a **Marburg** virus specific immune response;

(18) a panfilovirus vaccine comprising a mixture of **Ebola** virus (EBOV) and **Marburg** virus (MARV) VLPs; and

(19) a MARV vaccine protective against infection with MARV-Musoke, MARV-Ravn, and MARV-Ci67, comprising MARV VLPs consisting essentially of **GP** and VP40 from MARV-Musoke.

ACTIVITY - Virucide.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The **filovirus** virus-like particle (VLP) is useful in preparing a vaccine against **Ebola** or **Marburg** virus infection.

Dwg.0/21

L25 ANSWER 5 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2005-497889 [50] WPIDS
DNC C2005-151482
TI New **Ebola** or **Marburg** glycoprotein peptides comprises a linear domain encompassing F88 or a linear domain encompassing F159, useful as vaccines for preventing or treating hemorrhagic fever due to **Ebola** or **Marburg**.
DC B04 D16
IN MPANJU, O; WILSON, C A
PA (USSH) US DEPT HEALTH & HUMAN SERVICES
CYC 108
PI WO 2005063798 A1 20050714 (200550)* EN 62
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE

KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
US UZ VC VN YU ZA ZM ZW

ADT WO 2005063798 A1 WO 2004-US43360 20041223

PRAI US 2003-532677P 20031223

AB WO2005063798 A UPAB: 20050805

NOVELTY - A polypeptide comprises a linear domain encompassing F88 or a linear domain encompassing F159 or its functional equivalent, substantially in isolation from sequences naturally occurring adjacent to it in the **Ebola** or **Marburg** glycoprotein **(GP)**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a polynucleotide sequence encoding at least one polypeptide above;

(2) a vector comprising the nucleotide sequence of (1);

(3) a particle comprising the polypeptide of above;

(4) a method of making the polypeptide;

(5) a host cell transformed with a vector of (2);

(6) a vaccine suitable for use in the prevention and/or treatment of hemorrhagic fever due to **Ebola** or **Marburg,** the vaccine comprised of the polypeptide or polynucleotide above, or the vaccine further comprising a physiological carrier;

(7) a method of preventing and/or treating a human body for hemorrhagic fever due to **Ebola** or **Marburg;**

(8) a molecular decoy comprising a polypeptide not substantially larger than the smallest size needed to retain the elements of the binding site of the **Ebola** or **Marburg GP** protein for the susceptible host cell receptor having an amino acid sequence selected from the polypeptide above or its peptidomimetic;

(9) a kit for detecting naturally occurring antibodies to **Ebola** or **Marburg** glycoprotein comprising in compartmental form a compartment adapted to contain the polypeptide above; and

(10) a method for detecting naturally occurring antibodies to **Ebola** or **Marburg** glycoprotein.

ACTIVITY - Antipyretic. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The polypeptide is useful as a vaccine for the prevention and/or treatment of hemorrhagic fever due to **Ebola** or **Marburg.**

Dwg.0/8

L25 ANSWER 6 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

Full Text

AN 2005-497469 [50] WPIDS

DNC C2005-151248

TI Modified cyanovirin protein composition useful in the treatment of viral infection comprises protein having specific amino acid sequence.

DC A96 B04 D16

IN KERNS, W; LEVINE, H L

PA (OMNI-N) OMNIVIRAL THERAPEUTICS LLC

CYC 108

PI WO 2005058229 A2 20050630 (200550)* EN 32

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
US UZ VC VN YU ZA ZM ZW

ADT WO 2005058229 A2 WO 2004-US33230 20041008

PRAI US 2003-510060P 20031009

AB WO2005058229 A UPAB: 20050805

NOVELTY - An OVT102 (modified cyanovirin protein) composition (C1) comprising a protein having a sequence of 102 amino acids as given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a kit for anti-viral treatment comprising (C1), a container and instructions for use;

(2) a nucleic acid (N1) encoding (C1);

(3) a nucleic acid (N2) encoding a gene for expressing (C1) in gram-negative bacterium;

(4) manufacturing an antiviral protein involving expressing (N1) or (N2) in Escherichia Coli;

(5) an article comprising (C1) immobilized on a solid substrate;

(6) removing virus from bodily fluid involving contacting the fluid with the article, where the virus remains associated, and separating the article from the fluid;

(7) an antibody having affinity (at least 10-8 M) and specificity for an epitope comprising the N-terminus of (C1);

(8) a cell carrying a vector having sequence of 321 amino acids as given in the specification;

(9) a probiotic antiviral medicament for treating an epithelial

lactic acid bacterium such as Bacillus sp., Lactobacillus sp. or Sporolactobacillus sp.; and

(10) a kit for diagnosis of an enveloped virus comprising (C1), container, instruction for use and an antibody.

ACTIVITY - Virucide; Anti-HIV; Antiinflammatory; Hepatotropic.

Modified cyanovirin protein composition comprising methionine as an additional N-terminal amino acid was tested against strain of influenza as follows. MDCk cells were added to each well of 96-well flat bottom tissue culture plates. The plate including only cell (control) and the plate including cell and the composition (control) were assayed. The data showed an IC50 value of the composition was 1 - 20nM, which is higher compared to control.

MECHANISM OF ACTION - **Gp**-120 inhibitor.

USE - In the treatment of antiviral infection (e.g. influenza, AIDS, herpes I, herpes II, hepatitis, smallpox, chicken pox, severe acute respiratory syndrome or **ebola**) caused by retrovirus (such as influenza virus, an immunodeficiency virus (such as HIV-1 or HIV-2), a lymphotropic virus or a leukemia virus), a herpesvirus, a poxvirus, an African swine fever virus, a togavirus, a coronavirus, a flavivirus, a paramyxovirus, a rhabdovirus, an arenavirus or a bunyavirus in an animal (preferably human) (claimed).

ADVANTAGE - The protein has increased therapeutic index and decreased toxicity to an animal cell compared to cyanovirin. It has at least 10 (preferably 20, especially 50, particularly 100)% increase in antiviral activity i.e. increased affinity for **Gp**-120 of HIV.

Dwg.0/7

L25 ANSWER 7 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2005-483562 [49] WPIDS
DNC C2005-147882
TI Preventing and/or treating infectious disease caused by virus having mucin type (O binding) sugar chain, by inhibiting interaction of macrophage C type lectin on macrophage, and mucin type sugar chain on virus particle, in patient.
DC B04 D16
IN FUJIOKA, H; IRIMURA, T; KAWAOKA, Y; TAKADA, A
PA (UYTY) UNIV TOKYO
CYC 1
PI JP 2005187428 A 20050714 (200549)* 14
ADT JP 2005187428 A JP 2003-433766 20031226
PRAI JP 2003-433766 20031226
AB JP2005187428 A UPAB: 20050802

NOVELTY - Preventing and/or treating (M1) infectious disease caused by a virus having mucin type (O binding type) sugar chain, involves inhibiting an interaction of macrophage C type lectin (MGL) for galactose, present on a macrophage, and a mucin sugar chain present on a virus particle, in a patient in need of such treatment.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a pharmaceutical composition (PC) for (M1), comprising an effective dose of soluble form of MGL protein or specific binding partner with respect to MGL.

ACTIVITY - Virucide.

MECHANISM OF ACTION - Inhibitor of interaction between MGL on macrophage and mucin sugar chain on virus (claimed). In vitro analysis of the ability of anti-hMGL antibody in inhibiting the interaction between mucin sugar chain on **Ebola** virus and MGL present on a macrophage was analyzed as follows. The human chronic myeloid leukemia cell (k562) was cultured in RPMI 1640 medium. Recombinant virus was produced by introducing envelope glycoprotein of **Ebola** virus (Zaire strain) into the G protein region of vesicular stomatitis virus (VSV) lacking the G protein region. The K562 cells (expressing an anti-human MGL antibody, as a result of transformation using MGL gene plasmid) were infected with the produced recombinant virus. After 30 minutes, the infection rate was measured using fluorescence activated cell sorter (FACS). The results showed that the administration of anti-hMGL significantly decreases the infection rate of **Ebola** virus and effectively inhibits the interaction of mucin sugar chain on **Ebola** virus and MGL present on a macrophage.

USE - (M1) and PC are useful for preventing and/or treating viral infections by virus, preferably **Filoviridae** virus, and more preferably **Ebola** virus (claimed).

ADVANTAGE - (M1) is effective in preventing or treating infectious disease by virus, preferably **Ebola** virus.

DESCRIPTION OF DRAWING(S) - The figure is a graph representing the infection rate of Zaire glycoprotein (**GP**), Zaire **GP** Delta mucin and vesicular stomatitis virus G protein, as measured by fluorescence activated cell sorter. (Drawing includes non-English language text).

Dwg.1/3

L25 ANSWER 8 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2005-233265 [24] WPIDS

DNC C2005-073991
TI New isolated **GP**, NP, VP24, VP30, VP35 and VP40 **Ebola** peptides, useful in inducing an immune response which is protective against infection with the **Ebola** virus.
DC B04 D16
IN BAILEY, M A; HART, M K; OLINGER, G G; WILSON, J A
PA (USSA) US ARMY MEDICAL RES INST INFECTIOUS DISE
CYC 109
PI WO 2005023837 A2 20050317 (200524)* EN 110
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2004270611 A1 20050317 (200570)
EP 1608393 A2 20051228 (200603) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PL PT RO SE SI SK TR
ADT WO 2005023837 A2 WO 2004-US7185 20040309; AU 2004270611 A1 AU 2004-270611 20040309; EP 1608393 A2 EP 2004-775833 20040309, WO 2004-US7185 20040309
FDT AU 2004270611 A1 Based on WO 2005023837; EP 1608393 A2 Based on WO 2005023837
PRAI US 2003-384976 20030310
AB WO2005023837 A UPAB: 20060112
NOVELTY - An isolated **GP**, NP, VP24, VP30, VP35 and VP40 **Ebola** peptides comprising a fully defined sequence of 15, 11, 23, 15, 8 and 15 amino acids (SEQ ID NO: 29, 24, 25, 32, 34 and 37, respectively), or its peptide fragment comprising at least 9 consecutive amino acids, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated DNA fragment which encodes the **GP Ebola** peptide cited above;

(2) a DNA fragment which encodes the NP, VP24, VP30, VP35 and/or VP40 **Ebola** peptide cited above;

(3) a recombinant DNA construct comprising a vector, and at least one of the **Ebola** virus DNA fragments encoding a peptide selected from any of 20 fully defined sequences of 8-30 amino acids (SEQ ID NO: 24-53);

(4) a pharmaceutical composition comprising any of SEQ ID NO: 24-53;

(5) a vaccine against **Ebola** infection comprising a peptide or a virus replicon particles expressing at least one of the peptides with any of SEQ ID NO: 24-53, and their mixtures, in a carrier and/or adjuvant;

(6) inducing in a mammal a cytotoxic T lymphocyte response to an **Ebola** peptide, comprising administering to a mammal an immunogenic composition comprising a peptide with SEQ ID NO: 24-53, or a recombinant DNA construct that expressed a peptide with SEQ ID NO: 24-53, and their mixtures, in a carrier and/or adjuvant; and

(7) an immunogenic composition comprising **Ebola** peptides VP30, VP35 and VP40.

ACTIVITY - Virucide.

BALB/c and C57Bl/6 mice were injected subcutaneously with 2x106 IU of Venezuelan Equine Encephalitis (VEE) virus replicons encoding either the individual **Ebola** genes or Lassa NP. The results showed the identification of the protective mechanism induced by VRP vaccination, showing the role of T cells, and the ability to predict protection from in vitro assays, specifically the intracellular cytokine and chromium release assays.

MECHANISM OF ACTION - Vaccine.

USE - The methods and compositions of the present invention are useful in inducing an immune response, which is protective against infection with **Ebola** virus.

Dwg.0/4

L25 ANSWER 9 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2005-123291 [13] WPIDS
DNC C2005-040964
TI New recombinant virus comprising antigen sequence(s) heterologous to a recombinant virus that encodes a viral antigen from a pathogenic virus, useful as genetic vaccine for stimulating humoral immune response against **Ebola** virus.
DC B04 D16
IN GEISBERT, T W; JAHRLING, P B; NABEL, G J; SULLIVAN, N J
PA (USNA) US SEC OF NAVY
CYC 108
PI WO 2005012538 A2 20050210 (200513)* EN 40
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ

US UZ VC VN YU ZA ZM ZW
ADT WO 2005012538 A2 WO 2004-US24781 20040802
PRAI US 2003-491933P 20030801
AB WO2005012538 A UPAB: 20050224

NOVELTY - A recombinant virus comprising an antigen sequence(s) heterologous to the recombinant virus that encodes a viral antigen from a pathogenic virus, the recombinant virus being replication competent or replication defective adenovirus or related virus, is new.

DETAILED DESCRIPTION - A recombinant virus comprising an antigen sequence(s) heterologous to the recombinant virus that encodes a viral antigen from a pathogenic virus, expression of the viral antigen sequences eliciting an immune response directed against the viral antigen and cells expressing the viral antigen in the host upon infection of the host by the recombinant virus, the recombinant virus being replication competent or replication defective adenovirus or related virus, in single dose form, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) accelerated vaccination;

(2) a pharmaceutical composition comprising a first recombinant virus comprised of an antigen sequence heterologous to the recombinant virus that encodes a first viral antigen from a pathogenic virus, expression of the viral antigen eliciting an immune response directed against the viral antigen and cells expressing the viral antigen in the host upon infection of the host by the recombinant virus, the recombinant virus being replication competent or replication defective adenovirus or related virus, and a second recombinant virus comprised of an antigen sequence heterologous to the recombinant virus that encodes a second viral antigen from the same pathogenic virus, expression of the viral antigen eliciting an immune response directed against the viral antigen and cells expressing the viral antigen in the host upon infection of the host by the recombinant virus, the recombinant virus being replication competent or replication defective adenovirus or related virus, where the first viral antigen is a surface antigen and the second viral antigen is a core antigen; in single dose form; and

(3) a pharmaceutical composition comprising a recombinant virus comprised of antigen sequences heterologous to the recombinant virus, at least one encoding a first viral antigen from a pathogenic virus, and at least another encoding a second viral antigen from the same pathogenic virus, expression of the antigen sequences eliciting an immune response directed against the viral antigen and cells expressing the viral antigen in the host upon infection of the host by the recombinant virus, the recombinant virus being replication competent or replication defective adenovirus or related virus, where the first viral antigen is a surface antigen and the second viral antigen is a core antigen; in single dose form.

ACTIVITY - Virucide: Immunostimulant.

No biological data given.

MECHANISM OF ACTION - Vaccine.

No biological data given.

USE - The recombinant virus is useful as genetic vaccine for stimulating cellular and humoral immune responses in human and other hosts against **Ebola** virus. It is also useful for immunizing a host against a wide variety and different strains of pathogenic viruses such as HIV-1, HIV-2, herpes simplex virus type 1 and 2, influenza virus, **Marburg** virus, and hepatitis A, B, C, D, and E viruses. It is also useful for expressing multiple antigen sequences simultaneously from the same viral vector.

Dwg.0/4

L25 ANSWER 10 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-758332 [74] WPIDS
DNC C2004-266161
TI New peptides that specifically target and bind to dendritic cells (e.g. myeloid, Langerhans or plasmacytoid dendritic cells), useful for promoting an immune response against pathogenic viruses (e.g. HIV) or tumor cells.
DC B04 D16
IN CURIEL, T; MOHAMADZADEH, M; MORRIS, C
PA (TULA) TULANE EDUCATIONAL FUND
CYC 108
PI WO 2004092195 A2 20041028 (200474)* EN 77
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
US UZ VC VN YU ZA ZM ZW
ADT WO 2004092195 A2 WO 2004-US10832 20040408
PRAI US 2003-461474P 20030409
AB WO2004092195 A UPAB: 20041117

NOVELTY - A peptide that specifically targets and binds to a dendritic

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a fusion protein comprising the above peptide and a non-dendritic cell protein or its fragments;

(2) a (multivalent) vaccine delivery system comprising the peptide that specifically targets and binds to dendritic cells; and a virus specific protein, a bacteria specific protein, a tumor associated antigen, or their fragments; or at least 2 of the above peptides or virus specific proteins;

(3) a method of promoting an immune response in an individual in need of such treatment; and

(4) a DNA sequence encoding the above peptide or fusion protein.

ACTIVITY - Virucide; Anti-HIV; Cytostatic; Immunostimulant.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The composition and methods are useful for promoting an immune response in an individual against pathogenic viruses (e.g. HIV or **Ebola**) or against tumor cells (e.g. breast cancer).

Dwg.0/9

L25 ANSWER 11 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-667958 [65] WPIDS
CR 2002-122028 [16]; 2003-182621 [18]; 2003-851718 [79]; 2004-021936 [02]
DNC C2004-238627
TI Enhancing immunity to infection of a pathogenic virus, useful for preventing or treating viral or bacterial diseases, comprises administering a recombinant adenovirus comprising an antigen sequence heterologous to a native adenovirus.
DC B04 C06 D16
IN WANG, D
PA (WANG-I) WANG D
CYC 1
PI US 2004185064 A9 20040923 (200465)* 185
ADT US 2004185064 A9 CIP of US 2000-585599 20000602, CIP of WO 2001-US18238 20010604, CIP of US 2001-3035 20011101, US 2002-286332 20021101
FDT US 2004185064 A9 CIP of US 6544780
PRAI US 2002-286332 20021101; US 2000-585599 20000602;
WO 2001-US18238 20010604; US 2001-3035 20011101
AB US2004185064 A UPAB: 20041011

NOVELTY - Enhancing the immunity of a host to infection of a first and second pathogenic virus comprises administering to the host a recombinant adenovirus comprising an antigen sequence heterologous to native adenovirus and encodes a viral antigen from the pathogenic virus.

DETAILED DESCRIPTION - Enhancing the immunity of a host to infection of a first and second pathogenic virus comprises:

(a) administering to the host a first recombinant adenovirus comprising a first antigen sequence heterologous to native adenovirus and encoding a first viral antigen from the first pathogenic virus, expression of the first viral antigen by the first recombinant adenovirus eliciting an immune response directed against the first viral antigen in a host upon infection of the host by the first recombinant adenovirus; and

(b) administering to the host a second recombinant adenovirus comprising a second antigen sequence heterologous to native adenovirus and encoding a second viral antigen from the second pathogenic virus, expression of the second viral antigen by the second recombinant adenovirus eliciting an immune response directed against the second viral antigen in a host upon infection of the host by the first recombinant adenovirus.

ACTIVITY - Virucide; Antibacterial; Antiparasitic.

MECHANISM OF ACTION - Vaccine.

USE - The method is useful for enhancing the immunity of a host to infection of a first and second pathogenic virus. The method is useful preventing or treating diseases using the vaccines of the invention. The vaccines are useful against bacteria, viruses, or parasites, preferably against HIV infection, hepatitis viruses, or **Ebola** virus.

Dwg.0/63

L25 ANSWER 12 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-625495 [60] WPIDS
DNC C2004-225008
TI Decreasing infection of cell by virus, HIV, influenza A or **Ebola**, comprises interfering with activity or expression of host proteins or activity of host nucleic acids such as Rab9, AXL receptor tyrosine kinase, and Beta-chimerin .
DC B04 D16
IN HODGE, T W; MOREY, N J; RUBIN, D; SANCHEZ, A; SHAW, M W; HODGE, T; MOREY, N; SHAW, M
PA (USSH) US DEPT HEALTH & HUMAN SERVICES; (UYVA-N) UNIV VANDERBILT; (USNA) US SEC OF NAVY
CYC 108

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM
PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US
UZ VC VN YU ZA ZM ZW
AU 2003303308 A1 20040830 (200480)
EP 1613724 A2 20060111 (200604) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
MC MK NL PT RO SE SI SK TR

ADT WO 2004070002 A2 WO 2003-US37143 20031118; AU 2003303308 A1 AU 2003-303308 20031118; EP 1613724 A2 EP 2003-815298 20031118, WO 2003-US37143 20031118

FDT AU 2003303308 A1 Based on WO 2004070002; EP 1613724 A2 Based on WO 2004070002

PRAI US 2003-482604P 20030625; US 2002-427464P 20021118

AB WO2004070002 A UPAB: 20040920

NOVELTY - Decreasing infection of a host cell by a virus comprises interfering with an activity or expression of one or more host proteins or interfering with an activity of one or more host nucleic acids where the host protein or nucleic acid comprises Rab9, AXL receptor tyrosine kinase, Beta-chimerin and mammalian selenium binding protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) methods of decreasing HIV, **Ebola**, or influenza A infection of a host cell;

(2) a method of treating an HIV, **Ebola**, or influenza A viral infection in a host subject;

(3) a method of determining resistance or susceptibility to viral infection in a subject;

(4) a method of identifying a compound that decreases binding of a viral protein to a host protein and decreases viral infection;

(5) a method of decreasing infection of a host cell by a pathogen;

(6) a cell comprising a functional deletion of one or more target sequences associated with any of the 35 nucleotide sequences fully defined in the specification, where the cell has a decreased susceptibility to HIV infection;

(7) a cell comprising a functional deletion of one or more target sequences associated with any of the 27 nucleotide sequences fully defined in the specification, where the cell has a decreased susceptibility to influenza infection;

(8) a cell comprising a functional deletion of one or more target sequences associated with any of the 168 nucleotide sequences fully defined in the specification, where the cell has a decreased susceptibility to **Ebola** infection;

(9) a cell comprising a functional deletion of a Rab9 gene, where the cell has a decreased susceptibility to infection by a pathogen that uses lipid rafts; and

(10) a non-human transgenic mammal comprising any of the functional deletions cited above.

ACTIVITY - Virucide; Anti-HIV; Antibacterial.

MECHANISM OF ACTION - RNAi; RNA interference; Axl tryosine kinase receptor inhibitor; Rab9 inhibitor; beta chimerin inhibitor; retinoblastoma binding protein 1 inhibitor; protein cell control modulator; mammalian selenium binding protein inhibitor; KOX inhibitor.

Rab9, AXL (AXL receptor tyrosine kinase), CHN (Beta-chimerin), KOX, RBB (retinoblastoma binding protein 1), KIAA1259, F3 and mammalian selenium binding protein siRNA sequences were generated, pooled, hybridized to its appropriate complement sequence and used to transfect JC53 (HeLa cells modified to accept HIV), Vero (monkey kidney cells), MDCK (dog kidney cells, or HEK (human kidney cells). GFP siRNA sequences were used as negative controls.

Cells (20000 to 250000) were incubated in serum free media for 24 hours. Cocktails were made by mixing the siRNAs (50-100 pmoles) with lipofectamine 2000 (4-16 micro l) and RNAse inhibitor (1-4 micro l) in a solution of Optimem (serum free medium) in a total volume of 200-2000 micro l. Aliquots (50-500 micro l) of the cocktail were added to the cells which were incubated at 37 deg. C for 48 hours. The cells were then infected with HIV, **Ebola**, or influenza and the incubation continued for 3-7 days. Following transfection, several assays were conducted to confirm transfection efficiency and to determine the resistance of the cells to infection by various agents.

Quantitation of p24 levels of HIV infected J5C3 cells was determined. Rab9 siRNAs and mammalian selenium binding protein siRNAs each decreased HIV infection by 50% on day 4 post infection (day 7 post addition of siRNA). In addition, HIV infection decreased by 80-90% in the presence of beta-chimerin siRNAs, KOX siRNAs, or retinoblastoma binding protein 1 siRNA. However, HIV infection did not decrease in the presence of siRNAs that recognize KIAA1259, F3 or AXL siRNAs.

Infection of **Ebola** in HEK293 cells transfected with Rab9 or AXL siRNA was determined by measuring **gp1** antigen using fluorescent antibody to **gp1** envelope protein. Infection was decreased by 90-95% in presence

decreased by 80% in presence of AXL siRNA compared to absence.
USE - The method is useful for decreasing and treating infection of a host cell by a virus, such as HIV, influenza A or **Ebola** virus. Specifically, especially where the pathogen hijacks a lipid raft, the method is useful for decreasing infection of Campylobacter jejuni, Vibrio cholerae SV40, Legionella pneumophila, Aeromonas hydrophila, Echovirus 1, Echovirus 11, Brucella spp., Clostridium spp., Avian sarcoma and leukosis virus, FimH, Escherichia coli, Streptococcus pyogenes, Semliki forest virus, Salmonella typhimurium, Bacillus anthracis, Ecotropic mouse leukaemia virus, Shigella flexneri, Bacillus thuringiensis, HTLV-I, Chlamydia spp., Helicobacter pylori, HFV-I, Mycobacterium spp., Listeria monocytogenes, **Ebola**, **Marburg**, Measles, Herpes Simplex virus, influenza virus, or Epstein-Barr virus (claimed).
Dwg.0/6

L25 ANSWER 13 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-226835 [21] WPIDS
DNC C2004-089480
TI New isolated monoclonal antibody that binds **Ebola** virus **GP**, which monoclonal antibody comprises a heavy chain variable region, useful for treating or ameliorating **Ebola** virus infection.
DC B04 D16
IN HART, M K; WILSON, J; WILSON, J A
PA (USSA) US ARMY MEDICAL RES INST INFECTIOUS DISE; (HART-I) HART M K; (WILS-I) WILSON J; (USSA) US SEC OF ARMY
CYC 106
PI WO 2004018649 A2 20040304 (200421)* EN 68
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
US 2004053865 A1 20040318 (200421)
AU 2003265883 A1 20040311 (200457)
US 6875433 B2 20050405 (200523)
EP 1539238 A2 20050615 (200539) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
ADT WO 2004018649 A2 WO 2003-US27450 20030821; US 2004053865 A1 US 2002-226795 20020823; AU 2003265883 A1 AU 2003-265883 20030821; US 6875433 B2 US 2002-226795 20020823; EP 1539238 A2 EP 2003-793441 20030821, WO 2003-US27450 20030821
FDT AU 2003265883 A1 Based on WO 2004018649; EP 1539238 A2 Based on WO 2004018649
PRAI US 2002-226795 20020823
AB WO2004018649 A UPAB: 20040326
NOVELTY - An isolated monoclonal antibody that binds **Ebola** virus **GP**, which monoclonal antibody comprises a heavy chain variable region encoded by the DNA sequence having at least 90% homology to a sequence of 484, 504 or 511 bp fully defined in the specification, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a composition comprising the isolated **Ebola** virus monoclonal antibodies of an antibody produced by hybridoma EGP 13F6 accession number PTA 373, EGP 13C6-1-1 accession number PTA 375, and EGP 6D8-1-2 accession number PTA 376;
(2) a method for preventing **Ebola** virus infection in a mammal;
(3) a passive vaccine against **Ebola** virus infection comprising the composition cited above;
(4) a method of ameliorating an **Ebola** virus infection;
(5) a method for detecting **Ebola** virus in a sample;
(6) a kit for detecting **Ebola** virus in a biological sample comprising a container holding at least one monoclonal antibody selected from MAb 13F6, Mab13C6, and Mab 6D8; and instructions for using the at least one antibody for the purpose of binding to **Ebola** virus to form an immunological complex, and detecting the formation of the immunological complex such that presence or absence of immunological complex correlates with presence or absence of **Ebola** virus in the sample.
ACTIVITY - Virucide. No biologically data given.
MECHANISM OF ACTION - Immunotherapy.
USE - The monoclonal antibodies and compositions are useful for treating or ameliorating an **Ebola** virus infection (claimed).
Dwg.0/2

L25 ANSWER 14 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-083038 [08] WPIDS
DNC C2004-034154
TI New live replicating human spumavirus vector comprising an immunizing

treating viral, bacterial or parasitic infection or cancer.
DC B04 D16
IN CHEN, I S Y; FOLKS, T M; FOLKS, T
PA (USSH) US DEPT HEALTH & HUMAN SERVICES; (CHEN-I) CHEN I S Y; (FOLK-I) FOLKS T
CYC 104
PI WO 2004003153 A2 20040108 (200408)* EN 86
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003267976 A1 20040119 (200447)
EP 1572942 A2 20050914 (200560) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
US 2005244429 A1 20051103 (200573)
ADT WO 2004003153 A2 WO 2003-US20325 20030627; AU 2003267976 A1 AU 2003-267976 20030627; EP 1572942 A2 EP 2003-748923 20030627, WO 2003-US20325 20030627; US 2005244429 A1 Provisional US 2002-392630P 20020627, WO 2003-US20325 20030627, US 2005-519531 20050531
FDT AU 2003267976 A1 Based on WO 2004003153; EP 1572942 A2 Based on WO 2004003153
PRAI US 2002-392630P 20020627; US 2005-519531 20050531
AB WO2004003153 A UPAB: 20040202
NOVELTY - A live replicating human spumavirus vector (pHSV) for human use comprising an immunizing construct which partially replaces the bet gene, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a cell comprising the vector described above;
(2) detecting the expression of the vector;
(3) preventing or treating a subject with a condition;
(4) making a model useful in screening substances for treating or preventing a disease associated with an immunizing construct;
(5) a model from the method of (4);
(6) screening a substance for preventing or treating a disease associated with an immunizing construct; and
(7) screening for an immunizing construct for treating a disease associated with an immunizing construct.
ACTIVITY - Virucide; Antibacterial; Cytostatic. No biological data given.
MECHANISM OF ACTION - Gene Therapy.
USE - The vector is useful in preventing or treating a condition, e.g. viral, bacterial or parasitic infection or cancer.
Dwg.0/8

L25 ANSWER 15 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-011795 [01] WPIDS
DNC C2004-003463
TI New chimeric **Ebola** envelope protein comprising a functional **Ebola** glycoprotein binding domain fused to a heterologous amino acid sequence, useful for inducing an immune response against **Ebola** virus, bacteria, or fungi.
DC B04 C06 D16
IN KOBINGER, G; MEDINA, M F C; WILSON, J M
PA (UYPE-N) UNIV PENNSYLVANIA
CYC 103
PI WO 2003092582 A2 20031113 (200401)* EN 107
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003232004 A1 20031117 (200442)
US 2005255123 A1 20051117 (200576)
ADT WO 2003092582 A2 WO 2003-US11494 20030428; AU 2003232004 A1 AU 2003-232004 20030428; US 2005255123 A1 Provisional US 2002-376480P 20020430, Provisional US 2002-385704P 20020604, Provisional US 2002-427752P 20021120, WO 2003-US11494 20030428, US 2005-510947 20050111
FDT AU 2003232004 A1 Based on WO 2003092582
PRAI US 2002-427752P 20021120; US 2002-376480P 20020430; US 2002-385704P 20020604; US 2005-510947 20050111
AB WO2003092582 A UPAB: 20040102
NOVELTY - A chimeric **Ebola** envelope protein comprising a functional **Ebola** glycoprotein binding domain fused to a heterologous amino acid sequence, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the

(1) a nucleic acid molecule encoding a chimeric **Ebola** protein defined above;

(2) a host cell comprising the chimeric **Ebola** protein or nucleic acid molecule encoding the protein;

(3) a method of inducing an immune response against **Ebola** by delivering a composition comprising the chimeric **Ebola** protein or nucleic acid molecule encoding the protein;

(4) a recombinant virus having a chimeric **Ebola** envelope protein and a minigene;

(5) a host cell containing the recombinant virus;

(6) a method of treating a patient with a selected molecule by transducing the cells of the patient with the recombinant virus above;

(7) a method of delivering a molecule to the apical cells of the lung by administering a recombinant virus above intratracheally;

(8) an immunogenic composition comprising a DNA molecule encoding a chimeric **Ebola** envelope protein above under the control of sequences which direct its expression in a host cell, and a carrier; and

(9) an immunogenic composition comprising an **Ebola** envelope protein defined above, and a carrier.

ACTIVITY - Virucide; Antibacterial; Antiparasitic; Cytostatic.

MECHANISM OF ACTION - Vaccine. The cellular immune response to **Ebola** envelope in C57BL/6 mice was evaluated 8 days after a single intramuscular administration of 581010 particles of C7-LacZ or C7-**Ebola** envelope variant per animal. Mice were vaccinated with 5 multiply 1010 particles of C7 encoding LacZ or **Ebola** envelope variant. Splenic lymphocytes from immunized mice were collected 8 days post vaccination, and stimulated in vitro with feeder cells. standard 5-hour CTL assays were performed sing 51Cr-labeled syngeneic C57 cells transfected with an expressor of EboZ. A positive MHC-restricted cytotoxic T lymphocyte response was observed from all AdPan-7 encoding for **Ebola** envelope variants with a higher response from NTDL2, NTDL3 or NTDL4 immunized mice. Effector cells from C7 encoding **Ebola** envelope variant immunized mice recognized EboZ transfected target cells and gave recall CTL responses up to 30% specific lysis. Less than 5% lysis was seen with effector cells from naive or LacZ immunized control mice confirming that lysis was specific for **Ebola** envelope antigens.

USE - The recombinant virus is useful in preparing a medicament (claimed). The chimeric **Ebola** envelope protein is useful as an antigen for inducing an immune response against **Ebola** virus, and for generating a chimeric **Ebola**-pseudotyped virus, which delivers a selected molecule to a target cell. The proteins may be used to provide heterologous envelope to any vector derived from a viral source, which natively contain has an envelope. The protein may further be used to immunize a (non-)human animal against other pathogens including bacteria, fungi, parasitic microorganisms or multicellular parasites, which infect human and non-human vertebrates, or from a cancer or tumor cell.

Dwg.0/3

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L25  ANSWER 16 OF 29  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN   2003-853717 [79]   WPIDS
DNC  C2003-240668
TI   New composition comprising a vector having first or second cell membrane
     fusion-generating activity, useful for conferring antitumor immunity in an
     individual having malignant cells.
DC   B04 D16
IN   FU, X; ZHANG, X
PA   (FUXX-I) FU X; (ZHAN-I) ZHANG X; (BAYU) BAYLOR COLLEGE MEDICINE
CYC  104
PI   WO 2003082200   A2 20031009 (200379)* EN  155
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL
            PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU
            ZA ZM ZW
     US 2004009604   A1 20040115 (200406)
     AU 2003258060   A1 20031013 (200435)
     EP 1494613      A2 20050112 (200504)  EN
         R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
            MC MK NL PT RO SE SI SK TR
     JP 2005521398   W  20050721 (200549)      101
ADT  WO 2003082200 A2 WO 2003-US9287 20030326; US 2004009604 A1 Provisional US
     2002-367788P 20020327, Provisional US 2002-410024P 20020911, US
     2003-397635 20030326; AU 2003258060 A1 AU 2003-258060 20030326; EP 1494613
     A2 EP 2003-745618 20030326, WO 2003-US9287 20030326; JP 2005521398 W JP
     2003-579743 20030326, WO 2003-US9287 20030326
FDT  AU 2003258060 A1 Based on WO 2003082200; EP 1494613 A2 Based on WO
     2003082200; JP 2005521398 W Based on WO 2003082200
PRAI US 2002-410024P       20020911; US 2002-367788P      20020327;
     US 2003-397635        20030326
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NOVELTY - A new composition comprises a vector comprising a first or second cell membrane fusion-generating activity.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method of generating fusion between a first cell and a second cell;
(2) a method of destroying a malignant cell;
(3) a method of generating a cell membrane fusion-generating Herpes Simplex Virus (HSV) vector;
(4) a mammalian cell comprising the composition; and
(5) a method of increasing tumor antigen presentation in an individual having malignant cell.
ACTIVITY - Cytostatic. No biological data given.
MECHANISM OF ACTION - Gene therapy; Vaccine.
USE - The composition is useful for conferring antitumor immunity in an individual having malignant cells (claimed).
Dwg.0/19

L25 ANSWER 17 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2003-851718 [79] WPIDS
CR 2002-122028 [16]; 2003-182621 [18]; 2004-021936 [02]; 2004-667958 [65]
DNC C2003-239954
TI Enhancing the immunity of a host to infection of a first and second pathogenic virus, e.g. influenza, hepatitis, respiratory syncytial, or HIV infections comprises administering to the host a first and a second recombinant adenovirus.
DC B04 D16
IN WANG, D
PA (WANG-I) WANG D
CYC 1
PI US 2003138459 A1 20030724 (200379)* 185
ADT US 2003138459 A1 CIP of US 2000-585599 20000602, CIP of WO 2001-US18238 20010604, CIP of US 2001-3035 20011101, US 2003-286332 20030317
FDT US 2003138459 A1 CIP of US 6544780
PRAI US 2003-286332 20030317; US 2000-585599 20000602;
WO 2001-US18238 20010604; US 2001-3035 20011101
AB US2003138459 A UPAB: 20041011
NOVELTY - Enhancing the immunity of a host to infection of a first and second pathogenic virus comprising administering to the host a first and a second recombinant adenovirus, is new.
DETAILED DESCRIPTION - Enhancing the immunity of a host to infection of a first and second pathogenic virus comprising administering to the host a first recombinant host cell comprising a first antigen sequence heterologous to native adenovirus and encoding a first viral antigen from the first pathogenic virus, where the expression of the first antigen by the first recombinant adenovirus elicits an immune response directed against the first viral antigen in a host upon infection of the host by the first recombinant adenovirus. The method further comprises administering to the host a second recombinant adenovirus comprising a second antigen sequence heterologous to native adenovirus and encoding a second viral antigen from the second pathogenic virus, where the expression of the second viral antigen by the second recombinant adenovirus elicits an immune response directed against the second viral antigen in a host upon infection of the host by the first recombinant adenovirus.
ACTIVITY - Virucide; Anti-HIV; Hepatotropic.
No biological data given.
MECHANISM OF ACTION - Vaccine.
USE - The method is useful for enhancing immunity of the host to infections, e.g. influenza, **Ebola**, **Marburg**, Arbovirus, hepatitis, respiratory syncytial, herpes simplex or human papilloma virus, or HIV infections (claimed).
Dwg.0/63

L25 ANSWER 18 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2003-833605 [77] WPIDS
DNC C2003-234558
TI A composition for preventing or treating viral infections associated with high lethality and incapacity (e.g. **Ebola** virus) comprises a filamentous phage presenting a ligand on its surface, and a physiological excipient or diluent.
DC B04 D16
IN ABBOTT, R; BAIRD, A; LAROCCA, D
PA (SELE-N) SELECTIVE GENETICS INC
CYC 103
PI WO 2003086276 A2 20031023 (200377)* EN 82
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL

ZA ZM ZW
AU 2003222171 A1 20031027 (200436)
ADT WO 2003086276 A2 WO 2003-US10081 20030401; AU 2003222171 A1 AU 2003-222171 20030401
FDT AU 2003222171 A1 Based on WO 2003086276
PRAI US 2002-370360P 20020405
AB WO2003086276 A UPAB: 20031128
NOVELTY - A composition for treating a microbial infection comprising a filamentous phage presenting a ligand on their surface and a physiological excipient or diluent, where the filamentous phage comprises a heterologous nucleic acid sequence, where the sequence encodes an anti-microbial agent, and where the ligand binds to a group present on the surface of a cell, the group providing portal-level specificity, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method for delivery of an anti-microbial agent, comprising contacting a cell with the above-mentioned filamentous phage;
(2) a method for treating or slowing a microbial infection, comprising contacting a cell with the above-mentioned filamentous phage;
(3) a kit comprising a container, the filamentous phage cited above, and instructions for use of the filamentous phage in an anti-microbial context;
(4) a filamentous phage particle presenting a ligand on its surface, where the phage genome encodes a gene product under control of a promoter for use in treating a microbial infection;
(5) a method of identifying a microbial epitope involved in host cell attachment or internalization, comprising contacting one or more ligand displaying genetic package with cell(s), where the ligands comprise a microbial epitope, where the packages comprise a nucleic acid encoding a detectable product that is expressed upon internalization of the package, and where the cell(s) is/are capable of being infected by a microbe; detecting product expressed by the cell(s); and recovering a nucleic acid molecule encoding a microbial epitope from the cell(s), thus, identifying a microbial epitope involved in host cell attachment or internalization;
(6) a method of preventing microbial infection, comprising delivering a microbial epitope identified by the above method to a patient; and
(7) a method of inducing an immune response, comprising delivering a microbial epitope identified by the method in (5) to a patient.
ACTIVITY - Virucide. No biological data given.
MECHANISM OF ACTION - Gene therapy; Vaccine.
USE - The composition and methods are useful for portal specific gene delivery and prevention or treatment of microbial infections, particularly viral infections associated with high lethality and incapacity (e.g. **Ebola** or Variola virus). These may also be used for identifying epitopes and ligands capable of directing internalization of a vector and capable of blocking viral entry.
Dwg.0/0

L25 ANSWER 19 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2003-441461 [41] WPIDS
CR 2005-809991 [82]
DNC C2003-116869
TI New **filovirus** virus-like particle having an envelope glycoprotein and matrix protein, useful for diagnosing, preventing and/or treating **Ebola** and **Marburg** virus infections in humans and non-human primates.
DC B04 D16
IN AMAN, M J; BAVARI, S; SCHMALJOHN, A L
PA (USSA) US ARMY MEDICAL RES INST INFECTIOUS DISE; (AMAN-I) AMAN M J; (BAVA-I) BAVARI S; (SCHM-I) SCHMALJOHN A L
CYC 85
PI WO 2003039477 A2 20030515 (200341)* EN 61
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
US 2004057967 A1 20040325 (200422)
EP 1461424 A2 20040929 (200463) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
AU 2002352546 A1 20030519 (200464)
ADT WO 2003039477 A2 WO 2002-US35834 20021107; US 2004057967 A1 Provisional US 2001-338936P 20011107, US 2002-289839 20021107; EP 1461424 A2 EP 2002-789508 20021107, WO 2002-US35834 20021107; AU 2002352546 A1 AU 2002-352546 20021107
FDT EP 1461424 A2 Based on WO 2003039477; AU 2002352546 A1 Based on WO 2003039477
PRAI US 2001-338936P 20011107; US 2002-289839 20021107
AB WO2003039477 A UPAB: 20051222
NOVELTY - A new **filovirus** virus-like particle (VLP) comprises

(VP40), and is produced by expressing in a cell a polynucleotide encoding **GP** and VP40, such that the polynucleotide is expressed and VLP is produced.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for inhibiting the association of **GP** with lipid rafts, comprising inhibiting palmitoylation at cysteine residues 670 and 672 of the **GP**;

(2) a method for preventing **filovirus** trafficking into and out of a cell comprising disrupting lipid rafts of the cell or introducing cholesterol synthesis inhibitors to a cell;

(3) a **filovirus** vaccine comprising VLP and/or a nucleic acid encoding an agent capable of eliciting an immune response against the **filovirus**;

(4) a method for introducing an agent into a cell, comprising packaging the agent into a VLP producing a packed VLP and allowing the packed VLP to enter the cell;

(5) a method for testing an agent involved in **filovirus** budding, comprising introducing the agent to a cultured cell producing **filovirus** VLP and monitoring the presence or absence of a change in the budding of VLP as compared to a control by measuring VLPs in supernatant of the cultured cell, where a reduction or increase in the number of VLP in the supernatant indicates a negative or positive agent, respectively, on **filovirus** budding;

(6) a method for inhibiting **Ebola** virus infection in a cell, comprising administering raft-disrupting agents to the cell lipid;

(7) a method for detecting **Ebola** virus infection comprising contacting a sample from a subject suspected of having **Ebola** virus infection with an **Ebola** VLP, and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Ebola** VLP and antibodies specific for it in the sample;

(8) a kit for the detection of **Ebola** virus infection comprising **Ebola** VLPs;

(9) a method for detecting **Marburg** virus infection comprising contacting a sample from a subject suspected of having **Marburg** virus infection with a **Marburg** VLP, and detecting the presence or absence of an infection by detecting the presence or absence of a complex formed between the **Marburg** VLP and antibodies specific for it in the sample;

(10) a kit for the detection of **Marburg** virus infection comprising **Marburg** VLPs;

(11) a kit for testing agents involved in **Ebola** or **Marburg** budding, comprising a cell producing **Ebola** or **Marburg** VLPs and ancillary reagents for detecting VLPs in the supernatant of the cells when cells are cultured;

(12) an **Ebola** VLP-producing or **Marburg** VLP-producing cell comprising a mammalian cell expressing **Ebola GP** or **Marburg GP**, and VP40;

(13) an immunogenic composition comprising **Ebola** or **Marburg** VLPs in a vehicle; and

(14) a method for stimulating an **Ebola** or **Marburg** virus specific immune response, comprising administering to a subject an **Ebola** or **Marburg** VLPs in a vehicle.

ACTIVITY - Virucide.

Test details are described but nor results were given.

MECHANISM OF ACTION - Vaccine.

USE - The methods and compositions of the present invention of generating genome-free **Ebola** and/or **Marburg** VLPs, are useful for diagnosing, preventing and/or treating **Ebola** and **Marburg** virus infections in humans and non-human primates.

Dwg.0/9

L25 ANSWER 20 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2003-381622 [36] WPIDS
DNC C2003-101374
TI New recombinant respiratory syncytial virus with genes encoding the attachment, fusion and small hydrophobic proteins deleted, useful in molecular virology and vaccine development, and in methods of screening for antiviral agents.
DC B04 D16
IN MEGAW, A G; OOMENS, A T; WERTZ, G W; MEGAW, G; OOMENS, T A
PA (MEGA-I) MEGAW A G; (OOME-I) OOMENS A T; (WERT-I) WERTZ G W; (UABR-N) UAB RES FOUND
CYC 88
PI WO 2003029416 A2 20030410 (200336)* EN 80
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
US 2003072773 A1 20030417 (200340)
AU 2002343462 A1 20030414 (200461)

2001-326259P 20011001, Provisional US 2002-397289P 20020719, US 2002-262238 20021001; AU 2002343462 A1 AU 2002-343462 20021001
FDT AU 2002343462 A1 Based on WO 2003029416
PRAI US 2002-397289P 20020719; US 2001-326259P 20011001; US 2002-262238 20021001
AB WO2003029416 A UPAB: 20030609
NOVELTY - A recombinant respiratory syncytial virus (RSV) in which all of the surface glycoprotein genes encoding the attachment protein (G), the fusion protein (F), and the small hydrophobic protein (SH) are deleted and replaced by a gene encoding a heterologous protein that mediates cell infection and entry activity of the respiratory syncytial virus, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method of making a recombinant RSV that can infect a cell but cannot spread beyond the cell, comprising constructing a recombinant RSV in which all of the surface glycoprotein genes encoding protein G, protein F, and protein SH are deleted, and providing in trans a heterologous protein that mediates cell infection of the RSV, where the respiratory syncytial virus can infect a cell but cannot spread beyond the cell;
(2) a method of targeting a recombinant RSV, comprising constructing a recombinant RSV in which all of the surface glycoprotein genes encoding protein G, protein F, and SH are deleted, and incorporating a gene encoding a heterologous protein that mediates cell infection, entry, assembly, maturation and targeting of the RSV; and
(3) a method of testing immunogenicity of an epitope of the surface glycoproteins of RSV in a background of a live and transmissible virus, comprising constructing a recombinant RSV in which all of the surface glycoprotein genes encoding protein G, protein F, and protein SH are deleted, and incorporating a gene encoding the epitope into the recombinant RSV, where the recombinant RSV allows testing of the epitope in a background of a live and transmissible virus.
ACTIVITY - Virucide.
No biological data given.
MECHANISM OF ACTION - Vaccine.
USE - The methods and compositions of the present invention are useful in molecular virology and vaccine development. The recombinant RSV of the present invention is also useful in methods of screening for antiviral agents.
Dwg.0/11

L25 ANSWER 21 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2003-371961 [35] WPIDS
DNC C2003-098793
TI New bimodal priming and boosting compositions, useful as viral vaccines, specifically for eliciting an immune response against a **filovirus** or a disease caused by infection with **filovirus**.
DC B04 C06 D16
IN NABEL, G J; SANCHEZ, A; SULLIVAN, N; YANG, Z; NABEL, G
PA (USSH) US DEPT HEALTH & HUMAN SERVICES; (NABE-I) NABEL G; (SANC-I) SANCHEZ A; (SULL-I) SULLIVAN N; (YANG-I) YANG Z
CYC 102
PI WO 2003028632 A2 20030410 (200335)* EN 109
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2002327049 A1 20030414 (200460)
US 2004259825 A1 20041223 (200504)
EP 1504112 A2 20050209 (200512) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
JP 2005508916 W 20050407 (200524) 161
EP 1586331 A1 20051019 (200569) EN
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR
CA 2519282 A1 20030410 (200613) EN
ADT WO 2003028632 A2 WO 2002-US30251 20020924; AU 2002327049 A1 AU 2002-327049 20020924; US 2004259825 A1 Provisional US 2001-326476P 20011001, WO 2002-US30251 20020924, US 2004-491121 20040823; EP 1504112 A2 EP 2002-761814 20020924, WO 2002-US30251 20020924; JP 2005508916 W WO 2002-US30251 20020924, JP 2003-531968 20020924; EP 1586331 A1 Div ex EP 2002-761814 20020924, EP 2005-13732 20020924; CA 2519282 A1 Div ex CA 2002-2462455 20020924, CA 2002-2519282 20020924
FDT AU 2002327049 A1 Based on WO 2003028632; EP 1504112 A2 Based on WO 2003028632; JP 2005508916 W Based on WO 2003028632; EP 1586331 A1 Div ex EP 1504112
PRAI US 2001-326476P 20011001; US 2004-491121 20040823
AB WO2003028632 A UPAB: 20030603
NOVELTY - A bimodal priming composition and boosting composition for

new.

DETAILED DESCRIPTION - A bimodal priming composition and boosting composition comprises:

(a) a priming composition comprised of a DNA plasmid or a first genetic construct having a nucleic acid molecule encoding **Ebola, Marburg,** Lasso, retrovirus, paramyxovirus or influenza virus glycoprotein or nucleoprotein or their epitope-bearing domain, or a DNA plasmid selected from 43 6200-8300 nucleotide plasmid sequences, given in the specification, or their insert or analog having at least 95 % identity to them; and

(b) a boosting composition comprised of a replication-deficient adenovirus or a second genetic construct comprising a nucleic acid molecule encoding **Ebola Marburg,** Lasso, retrovirus, paramyxovirus, or influenza virus glycoprotein or nucleoprotein or epitope-bearing domain, or a replication deficient adenovirus selected from 43 constructs defined in the specification, their insert or analog having at least 95 % identity.

The first genetic construct is consists plasmid DNA, replication-deficient adenovirus or vaccinia virus, recombinant avipox virus or recombinant herpes virus. The second genetic construct consists of replication-deficient adenovirus or vaccinnia virus, recombinant avipox virus, or recombinant herpes virus. The bimodal boosting and priming composition is for the production of the antigen by expression from the first genetic construct and second genetic construct or from the DNA plasmid and replication-deficient adenovirus, where an immune response to the antigen previously primed in the individual is boosted.

INDEPENDENT CLAIMS are also included for methods of boosting or inducing an immune response to an antigen in an individual.

ACTIVITY - Virucide.

No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The bimodal boosting and priming composition is useful as viral vaccines, specifically for eliciting an immune response against a **filovirus** or a disease caused by infection with **filovirus.**

Dwg.0/51

L25 ANSWER 22 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2003-040651 [03] WPIDS
DNC C2003-009637
TI New chimeric **filovirus** glycoprotein (**GP**) protein comprising **GP1** and **GP2,** useful for inducing an immune response against infection of different **filoviruses,** specifically against both **Ebola** and **Marburg** viruses.
DC B04 D16
IN GROGAN, C C; HEVEY, M C; SCHMALJOHN, A L
PA (GROG-I) GROGAN C C; (HEVE-I) HEVEY M C; (SCHM-I) SCHMALJOHN A L; (USSA) US ARMY MEDICAL RES INST INFECTIOUS DISE
CYC 84
PI WO 2002079239 A2 20021010 (200303)* EN 94
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
US 2003108560 A1 20030612 (200340)
AU 2002303086 A1 20021015 (200432)
ADT WO 2002079239 A2 WO 2002-US3339 20020131; US 2003108560 A1 Provisional US 2001-267522P 20010131, US 2002-66506 20020131; AU 2002303086 A1 AU 2002-303086 20020131
FDT AU 2002303086 A1 Based on WO 2002079239
PRAI US 2001-267522P 20010131; US 2002-66506 20020131
AB WO 200279239 A UPAB: 20030113

NOVELTY - A chimeric **filovirus** glycoprotein (**GP**) protein comprising **GP1** and **GP2,** where **GP1** is from a **filovirus** different than that of **GP2,** is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a DNA fragment encoding a chimeric protein above and comprising a sequence of 2252, 1841, 2046 or 2246 bp given in the specification, or their conservative substitutions;

(2) a recombinant DNA construct comprising a vector, and a DNA fragment encoding a chimeric **filovirus GP** protein defined above;

(3) self replicating RNA produced from the construct of (2);

(4) infectious alphavirus particles produced from packaging the self replicating RNA of (3);

(5) a pharmaceutical composition comprising infectious alphavirus particles in a pharmaceutical carrier and/or adjuvant;

(6) a host cell transformed with a recombinant DNA construct;

(7) producing chimeric **filovirus GP** proteins by culturing the cells under conditions such that the DNA fragment is expressed and the

(8) a vaccine for more than one **filovirus** comprising viral particles containing one or more replicon RNA encoding chimeric **GP** from one or more **filovirus**;

(9) vaccines against **Ebola** and **Marburg** virus infections comprising a chimeric **GP** protein above, of infectious alphavirus particles produced from replicating RNA produced from the construct above;

(10) a pharmaceutical composition comprising a chimeric peptide encoded by any of the DNA sequences above, in a pharmaceutical carrier and/or adjuvant;

(11) a bivalent **filovirus** vaccine antigen comprising a chimeric **GP** protein comprising **GP1** or its portion, from a first **filovirus** and **GP2** or its portion from a second **filovirus**, where the antigen is able to elicit an immune response to 2 **filoviruses** in a subject; and

(12) a multivalent **filovirus** vaccine antigen comprising a chimeric **GP** protein where **GP1** and **GP2** are comprised of portions of **GP1** and **GP2** from different **filoviruses**, where the antigen able to elicit an immune response to more than 2 **filoviruses** in a subject.

ACTIVITY - Virucide. No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The chimeric **filovirus GP** protein is useful for inducing an immune response against infection of different **filoviruses**, specifically against both **Ebola** and **Marburg** viruses.

ADVANTAGE - The single-component bivalent vaccine comprising the chimeric **filovirus GP** protein is cost-effective, easy to produce, develop and test, and provides a protective immune response to multiple **filovirus** agents in a single component.

Dwg.0/10

L25 ANSWER 23 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

Full Text

AN 2002-122028 [16] WPIDS

CR 2003-182621 [18]; 2003-851718 [79]; 2004-021936 [02]; 2004-667958 [65]

DNC C2002-037345

TI Replication-incompetent recombinant virus useful as vaccine for immunizing humans against pathogenic virus, bacteria and parasites, has antigens heterologous to the virus and an immuno-stimulator sequence.

DC B04 D16

IN WANG, D; DONG, J

PA (GENP-N) GENPHAR INC; (WANG-I) WANG D

CYC 97

PI WO 2001091536 A2 20011206 (200216)* EN 142
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001071288 A 20011211 (200225)
EP 1286694 A2 20030305 (200319) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 6544780 B1 20030408 (200327)
CN 1446102 A 20031001 (200382)
JP 2003534016 W 20031118 (200401) 130
US 2004028652 A1 20040212 (200412)
ZA 2002009676 A 20040225 (200419) 154
US 6964762 B2 20051115 (200575)

ADT WO 2001091536 A2 WO 2001-US18238 20010604; AU 2001071288 A AU 2001-71288 20010604; EP 1286694 A2 EP 2001-950275 20010604, WO 2001-US18238 20010604; US 6544780 B1 US 2000-585599 20000602; CN 1446102 A CN 2001-813831 20010604; JP 2003534016 W JP 2001-587560 20010604, WO 2001-US18238 20010604; US 2004028652 A1 Div ex US 2000-585599 20000602, US 2002-327294 20021219; ZA 2002009676 A ZA 2002-9676 20021128; US 6964762 B2 Div ex US 2000-585599 20000602, US 2002-327294 20021219

FDT AU 2001071288 A Based on WO 2001091536; EP 1286694 A2 Based on WO 2001091536; JP 2003534016 W Based on WO 2001091536; US 2004028652 A1 Div ex US 6544780; US 6964762 B2 Div ex US 6544780

PRAI US 2000-585599 20000602; US 2002-327294 20021219

AB WO 200191536 A UPAB: 20051122

NOVELTY - A replication-incompetent recombinant virus (RV) comprising antigen sequences heterologous to RV, each sequence encoding a bacterial, viral or parasitic antigen whose expression elicits immune response against the antigen and cells expressing the antigen in a host upon infection of host by RV, and an immuno-stimulator (IS) sequence heterologous to RV, is new.

DETAILED DESCRIPTION - A replication-incompetent recombinant virus (RV) comprising antigen sequences heterologous to RV, each sequence encoding a bacterial, viral or parasitic antigen whose expression elicits immune response against the antigen and cells expressing the antigen in a host upon infection of host by RV, and an immuno-stimulator (IS) sequence heterologous to RV, is new. The IS sequence's expression in the host enhances the immunogenicity of the antigen, and RV does not cause a

ACTIVITY - Virucide; Antibacterial; Antiparasitic; Protozoacide; Anti-HIV.
MECHANISM OF ACTION - Vaccine.
The immune responses of animals to the adenoviral vaccine against HIV antigens was studied. Experimental mice were inoculated with the adenoviral vaccine, Ad.tat.env.IL2. Groups of C57BL/6 mice were injected intramuscularly with 107 plaque forming units (pfu) Ad.tat.env.IL2 on different dates. Blood was collected from four animals every two weeks following inoculation and serum was prepared. At 77 days post-inoculation, these mice were re-challenged with an additional 107 pfu of Ad.tat.env.IL2. Blood was collected from three animals every day following secondary challenge. Titers of antibody elicited against HIV tat and env were determined by enzyme linked immunosorbent assay (ELISA) against Ad.tat.env.IL2-infected HeLa cell lysates. The results showed that three mice in this group had strong immune responses to the HIV antigens expressed by the adenoviral vector Ad.tat.env.IL2, with the highest titer of antibody against HIV antigens reached in 42 days post inoculation. The second inoculation with Ad.tat.env.IL2 boosted the immune response again and very high titers were achieved within 5 days of the second inoculation.
USE - RV is useful for enhancing the immunity of a host to one or more pathogenic bacteria such as Bacillus tuberculosis, B. anthracis, spirochete, Borrelia burgdorferi that causes the Lyme disease in animals, parasites such as malaria, Cryptosporidium, Eimeria, Histomonas, Leucocytozoon, Plasmodium, Toxoplasma, Trichomonas, Leishmania, Trypanosoma, Giardia, Babesia or Theileria, and pathogenic viruses such as HIV type 1 and type 2, influenza virus, respiratory syncytial virus, herpes simplex virus type 1 and type 2, human papilloma virus, **Ebola** virus, **Marburg** virus and hepatitis A, B, C, D and E virus (claimed). The host is a human.
ADVANTAGE - RV induces a strong and long-lasting immune response to various strains or types of pathogens in the host.
Dwg.0/15

L25 ANSWER 24 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2001-235096 [24] WPIDS
DNN N2001-168082 DNC C2001-070459
TI Novel monoclonal antibody against epitopes on the **Ebola** virus glycoprotein useful as vaccines for detection, prevention and/or therapeutical treatment of **Ebola** virus infections.
DC B04 D16 S03
IN HART, M K; SCHMALJOHN, A L; WILSON, J A
PA (USSA) US ARMY MEDICAL RES INST INFECTIOUS DISE; (USSA) US SEC OF ARMY
CYC 83
PI WO 2001016183 A1 20010308 (200124)* EN 62
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 2000070896 A 20010326 (200137)
US 6630144 B1 20031007 (200374)
ADT WO 2001016183 A1 WO 2000-US23790 20000829; AU 2000070896 A AU 2000-70896 20000829; US 6630144 B1 Provisional US 1999-151505P 19990830, US 2000-650086 20000829
FDT AU 2000070896 A Based on WO 2001016183
PRAI US 1999-151505P 19990830; US 2000-650086 20000829
AB WO 200116183 A UPAB: 20010502
NOVELTY - An antibody (I) which recognizes **Ebola** virus glycoprotein (EVGP), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an antibody (II) which competes with (I) for binding to EVGP;
(2) a mixture (III) comprising **Ebola** virus antibodies comprising antibodies produced by hybridomas EGP 13F6-1-2 accession no. PTA 373, EGP 6D3-1-1 accession no. PTA 374, EGP 13C6-1-1 accession no. PTA 375, EGP 6D8-1-2 accession no. PTA 376, and/or EGP 12B5-1-1 accession no. PTA 436;
(3) a therapeutic composition (C) for ameliorating symptoms of **Ebola** virus infection, comprising (III);
(4) a passive vaccine against **Ebola** virus infection comprising (III);
(5) a monoclonal antibody producing cell line that produces (I);
(6) an anti-**Ebola** composition, comprising (I);
(7) a kit for detecting **Ebola** virus in a biological sample, comprising a container holding MAb 13F6, MAb 6D3, MAb 13C6, MAb 6D8, and/or MAb 12B5, and instructions for use;
(8) a vaccine for **Ebola** virus comprising one or more antigenic peptide epitopes recognized by MAb;
(9) a pharmaceutical composition comprising a peptide encoded by a 105 or 295 residue amino acid sequence (S1), fully defined in the specification, or a sequence (S2);

(11) an **Ebola** virus vaccine comprising (IV).
(S2) is AlaThrGlnValGluGlnHisHisArgArgThrAspAsnAspSerThrAla, GluGlnHisHisArgArgThrAspAsn, HisAsnThrProValTyrLysLeuAspIleSerGluAlaThrGlnValGlu, ValTyrLysLeuAspIleSerGluAla, GlyLysLeuGlyLeuIleThrAsnThrIleAlaGlyValAlaGlyLeuIle, or LeuIleThrAsnThrIleAlaGlyVal.
ACTIVITY - Antiviral.
MECHANISM OF ACTION - Vaccine.
Protective efficacy of (I) was determined by evaluating purified monoclonal antibodies for their ability to protect BALB/c mice from a lethal **Ebola** challenge. Groups of 5 mice/experiment were injected intraperitoneally with 100, 50 and 25 micro g of (I) in phosphate buffered saline, 1 day before, or 1 or 2 days after challenge with 300 times the lethal dose for 50 % adult mice (10 plaque forming units). All the monoclonal antibodies demonstrated protective efficacy when administered 1 day prior to or after challenge.
USE - (III) is useful for preventing **Ebola** virus infection in a subject. (I) is useful for inhibiting and ameliorating symptoms of **Ebola** virus infection. (I) is useful for detecting **Ebola** virus in a sample, by incubating the sample with (I), and detecting the complex, the presence or absence of the complex indicates the presence or absence of **Ebola** virus in the sample. (I) is also useful for treating **Ebola** virus infection. (All claimed).
Dwg.0/2

L25 ANSWER 25 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2000-224145 [19] WPIDS
DNC C2000-068326
TI New saponin derivatives with substituted triterpene aglycone core, used to potentiate antigens in vaccines against bacteria, viruses, protozoa and tumors.
DC A96 B01 B03 C02 D16
IN MARCIANI, D J; PRESS, J B
PA (MARC-I) MARCIANI D J; (PRES-I) PRESS J B; (GALE-N) GALENICA PHARM INC
CYC 23
PI WO 2000009075 A2 20000224 (200019)* EN 99
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP NO
AU 9955655 A 20000306 (200030)
US 6262029 B1 20010717 (200142)
ADT WO 2000009075 A2 WO 1999-US18635 19990813; AU 9955655 A AU 1999-55655 19990813; US 6262029 B1 Provisional US 1998-96691P 19980814, US 1999-373660 19990813
FDT AU 9955655 A Based on WO 2000009075
PRAI US 1998-96691P 19980814; US 1999-373660 19990813
AB WO 200009075 A UPAB: 20000419
NOVELTY - Saponin derivatives comprising a triterpene aglycone core substituted at positions 3 and 28 with a mono-or oligosaccharide are new.
DETAILED DESCRIPTION - A compound comprising a triterpene aglycone core wherein the core has a mono or oligo-saccharide covalently attached at position 3, a fucosyl residue covalently attached at position 28, wherein the fucosyl residue is optionally substituted with a mono- or oligo-saccharide and has a lipophilic group other than 3,5-dihydroxy-6-methyloctanoyl covalently attached to the 4 position, and a formyl or formylmethyl group covalently attached to the core at a position other than the 3 or 28 position.
An INDEPENDENT CLAIM is also included for a vaccine for human or veterinary use which comprises:
(a) one or more bacterial, viral, protozoal or tumor associated antigens; and
(b) one or more of the claimed saponin derivatives.
ACTIVITY - Immunopotentiators.
MECHANISM OF ACTION - None given.
USE - (I) are used as adjuvants in vaccine compositions used to vaccinate against bacteria, viruses, protozoa or tumors.
Dwg.0/2

L25 ANSWER 26 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2000-160677 [14] WPIDS
CR 2000-160676 [14]; 2005-233265 [24]
DNN N2000-119889 DNC C2000-050164
TI New **GP**, NP, VP24, VP30, VP35 and VP40 **Ebola** virus proteins, useful for prevention, treatment or diagnosis of **Ebola** infection, particularly where expressed from virus replicons.
DC B04 D16 S03
IN HART, M K; PUSHKO, P; SCHMALJOHN, A L; SMITH, J F; WILSON, J A; BAILEY, M A; OLINGER, G G
PA (USME-N) US MEDICAL RES INST INFECTIOUS DISEASES; (HART-I) HART M K; (PUSH-I) PUSHKO P; (SCHM-I) SCHMALJOHN A L; (SMIT-I) SMITH J F; (WILS-I) WILSON J A; (BAIL-I) BAILEY M A; (OLIN-I) OLINGER G G; (USSA) US SEC OF ARMY

PI   WO 2000000617   A2 20000106 (200014)* EN   70
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ UG ZW
         W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
            GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
            LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
            TT UA UG US UZ VN YU ZA ZW
     AU 9950844   A 20000117 (200026)
     EP 1119627   A2 20010801 (200144) EN
         R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
     US 2002164582   A1 20021107 (200275)
     US 2003224015   A1 20031204 (200380)
     AU 767147   B 20031030 (200382)
     US 2004146859   A1 20040729 (200450)
     US 6984504   B2 20060110 (200604)

ADT WO 2000000617 A2 WO 1999-US14311 19990622; AU 9950844 A AU 1999-50844 19990622; EP 1119627 A2 EP 1999-935350 19990622, WO 1999-US14311 19990622; US 2002164582 A1 Provisional US 1998-91403P 19980629, US 1999-337946 19990622; US 2003224015 A1 Provisional US 1998-91403P 19980629, CIP of US 1999-337946 19990622, US 2003-384976 20030310; AU 767147 B AU 1999-50844 19990622; US 2004146859 A1 Provisional US 1998-91403P 19980629, Cont of US 1999-337946 19990622, US 2003-696633 20031029; US 6984504 B2 Provisional US 1998-91403P 19980629, Cont of US 1999-337946 19990622, US 2003-696633 20031029

FDT AU 9950844 A Based on WO 2000000617; EP 1119627 A2 Based on WO 2000000617; AU 767147 B Previous Publ. AU 9950844, Based on WO 2000000617

PRAI US 1998-91403P   19980629; US 1999-337946   19990622;
     US 2003-384976   20030310; US 2003-696633   20031029

AB   WO 200000617 A UPAB: 20060116

NOVELTY - **GP**, NP, VP24, VP30, VP35 and VP40 **Ebola** virus proteins (or their immunologically identifiable portions) comprising sequences (I)-(VII) (where VP30 can be encoded by sequences (IV) and/or (V)) of 251-739 amino acids (aa), are new (all sequences are fully defined in the specification).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) DNA sequences (VIII)-(XIV) of 847-2428 nucleotides (nt), or their fragments of at least 15 nt and/or which encode at least 5 aa of sequences (I)-(VII), encoding a **GP**, NP, VP24, VP30, VP35 or VP40 **Ebola** virus protein (where VP30 can be encoded by (XI) and/or (XIV));

(2) a recombinant DNA construct (A) containing, in a vector, at least one of sequences (VIII)-(XIV) or their fragments of at least 15 nt;

(3) self-replicating RNA (B) produced by any one of EboVP24ReP, EboVP30ReP, EboVP35ReP, EboVP40ReP, EboVPNPReP, EboVPGPReP or EboVP30ReP (constructs of (A));

(4) infectious alphavirus particles (C) produced by packaging (B);

(5) prokaryotic/eukaryotic host cells (D) transformed with (A);

(6) production of **Ebola** virus proteins by culturing (D);

(7) antibodies (Ab) (E) raised against peptides of sequences (I)-(VII) and sequences of 11 and 23 amino acids (XV)-(XVI) respectively;

(8) detecting **Ebola** virus infection by formation of immune complex with (E);

(9) detecting **Ebola GP** RNA by polymerase chain reaction (PCR), using primers derived from (VIII);

(10) a diagnostic kit (F) for **Ebola** infection comprising fragments of at least 12 consecutive nt from (VIII) specific for the amplification of DNA or RNA of **Ebola** virus by PCR amplification plus ancillary reagents for detection; and

(11) a vaccine comprising (C);

All sequences are fully defined in the specification

ACTIVITY - Antiviral.

Capped replicon RNAs, from **Ebola** protein VP24, were produced by in vitro T7 run-off transcription of linearized plasmids and used, together with two helper RNAs expressing the structural proteins of Venezuelan equine encephalitis (VEE) virus, to transfect baby hamster kidney cells. Recombinant VEE virus replicons were recovered from the culture supernatant by centrifugation through a 20% sucrose solution. Balb/c mice were injected twice with 2 million focus-forming units of the resulting replicons (designated EboVP24VRP), then 1 month after the second injection challenged with 105 plaque-forming units of mouse-adated **Ebola** virus. All animals survived the challenge, compared with none of unvaccinated controls. Another example shows that immune serum from animals vaccinated with a replicon based on the **GP** protein (but not those based on other **Ebola** proteins) passively protected unvaccinated mice against challenge.

MECHANISM OF ACTION - Vaccine.

USE - (A) are useful to produce the following:

(1) the **Ebola** virus proteins as described above;

(2) self-replicating RNA; or

(3) infectious alphavirus particles;

all of which (also the constructs themselves) are useful in pharmaceutical compositions and protective vaccines. The **Ebola** proteins are also useful for the diagnosis of **Ebola** infection (by detecting

detect the proteins. DNA sequences (VIII)-(XIV) are useful as probes and primers for diagnostic hybridization or polymerase chain reaction assays for detecting **Ebola** virus (all claimed).
Dwg.0/4

L25 ANSWER 27 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2000-160676 [14] WPIDS
CR 2000-160677 [14]
DNC C2000-050163
TI Novel **Marburg** virus vaccines used to induce an immune response against the infection in nonhuman primates.
DC B04 D16
IN HEVEY, M C; NEGLEY, D L; PUSHKO, P; SCHMALJOHN, A L; SMITH, J F
PA (USME-N) US MEDICAL RES INST INFECTIOUS DISEASES; (HEVE-I) HEVEY M C; (NEGL-I) NEGLEY D L; (PUSH-I) PUSHKO P; (SCHM-I) SCHMALJOHN A L; (SMIT-I) SMITH J F; (USSA) US SEC OF ARMY
CYC 82
PI WO 2000000616 A2 20000106 (200014)* EN 57
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9947090 A 20000117 (200026)
EP 1092031 A2 20010418 (200123) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6517842 B1 20030211 (200314)
US 2003152590 A1 20030814 (200355)
AU 767551 B 20031113 (200381)
ADT WO 2000000616 A2 WO 1999-US14174 19990621; AU 9947090 A AU 1999-47090 19990621; EP 1092031 A2 EP 1999-930580 19990621, WO 1999-US14174 19990621; US 6517842 B1 Provisional US 1998-91403P 19980629, US 1999-336910 19990621; US 2003152590 A1 Provisional US 1998-91403P 19980629, Div ex US 1999-336910 19990621, US 2002-267322 20021009; AU 767551 B AU 1999-47090 19990621
FDT AU 9947090 A Based on WO 2000000616; EP 1092031 A2 Based on WO 2000000616; US 2003152590 A1 Div ex US 6517842; AU 767551 B Previous Publ. AU 9947090, Based on WO 2000000616
PRAI US 1998-91403P 19980629; US 1999-336910 19990621; US 2002-267322 20021009
AB WO 200000616 A UPAB: 20031216
NOVELTY - **Marburg** virus (MBGV) vaccines are new.
DETAILED DESCRIPTION - A novel recombinant DNA construct (I) comprises a vector, and at least one copy of the MBGV DNA fragments encoding **GP**, NP, VP40, VP35, VP30, VP24 and **GP** Delta TM proteins.
INDEPENDENT CLAIMS are also included for the following:
(1) self-replicating RNA produced from (I);
(2) a composition comprising infectious alphavirus particles of (1) in a carrier and/or adjuvant;
(3) a host cell transformed with (I);
(4) producing MBGV proteins by culturing the host cells of (3) to express the DNA fragment and ptoduce the protein;
(5) a vaccine for MBGV, comprising viral particles containing one or more replicon RNAs encoding one or more **GP**, NP, VP40, VP35, VP30, VP24 and **GP** Delta TM proteins;
(6) a composition, comprising one or more recombinant DNA constructs chosen from pRep Mus **GP**, pRep Mus NP, pRep Mus VP40, pRep Mus VP35, pRep Mus VP30, pRep Mus VP24 or pRep Mus **GP** Delta TM, in a carrier and/or adjuvant.
USE - The replicons and vectors and constructs are used to produce vaccines against **Marburg** virus (MBGV) infection (**Marburg** hemorrhagic fever) in mammals, to elicit immune responses against MBGV antigens, to confer protective immunity, and to reduce disease symptoms and reduce the severity of disease.
ADVANTAGE - The vaccine is efficient in protecting humans against MBGV.
Dwg.0/12

L25 ANSWER 28 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 1999-468944 [39] WPIDS
DNC C1999-137535
TI Solid nanospheres for genetic immunization of mammals, to raise immune response to antigen by cell-mediated and humoral immune responses.
DC A96 B04 D16
IN AUGUST, J T; LEONG, K W; TRUONG, V
PA (UYJO) UNIV JOHNS HOPKINS
CYC 85
PI WO 9936089 A1 19990722 (199939)* EN 33
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG US UZ VN YU ZW
AU 9921172 A 19990802 (199954)
EP 1045699 A1 20001025 (200055) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
AU 743226 B 20020124 (200221)
JP 2002509116 W 20020326 (200236) 33
NZ 505876 A 20021220 (200309)

ADT WO 9936089 A1 WO 1999-US860 19990115; AU 9921172 A AU 1999-21172 19990115; EP 1045699 A1 EP 1999-901486 19990115, WO 1999-US860 19990115; AU 743226 B AU 1999-21172 19990115; JP 2002509116 W WO 1999-US860 19990115, JP 2000-539862 19990115; NZ 505876 A NZ 1999-505876 19990115, WO 1999-US860 19990115

FDT AU 9921172 A Based on WO 9936089; EP 1045699 A1 Based on WO 9936089; AU 743226 B Previous Publ. AU 9921172, Based on WO 9936089; JP 2002509116 W Based on WO 9936089; NZ 505876 A Based on WO 9936089

PRAI US 1998-71746P 19980116

AB WO 9936089 A UPAB: 19990928

NOVELTY - New solid nanospheres of less than 5 mu m for genetic immunization of mammals comprising coacervate of polymeric cation and polyanion of nucleic acids, where at least a portion of the nucleic acids encode an antigen, and where a cytokine is encapsulated in coacervate.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) A method of immunizing a mammal to raise an immune response to an antigen comprising administering to a mammal a solid nanosphere as defined above; and

(2) a method of forming solid nanospheres for immunization of a mammal, comprising forming solid nanospheres by coacervation of a polyanion consisting of nucleic acids encoding an antigen and a polymeric cation, where the coacervation is done in the presence of a cytokine which is encapsulated in the solid spheres.

ACTIVITY - Antiviral; antibacterial; anti-tumor.

BALB/c mice (8 weeks) were divided into groups of 10. The mice were immunized by intramuscular injection in the tibialis anterior with three monthly injections of nanospheres containing 0.5 or 3 mu g nanosphere DNA encoding **Ebola** nucleoprotein (NP); 0.5 or 3 mu g nanosphere DNA encoding **Ebola** envelope glycoprotein (**GP**) antigens or 3 mu g control WRG7077 pDNA (vector without the **Ebola** NP or **GP** insert). The mice then were challenged with 30 multiply LD50 of mouse-adapted live **Ebola** Zaire strain. Survival rates were tabulated at week 12. No deaths were observed after day 10. The survival rate was better with each antigen than with vector control and was significantly greater with the higher dose (p less than 0.05). A higher degree of protection was achieved with **Ebola** NP vaccination than with **Ebola GP** (90% versus 40%). The geometric means anti-**GP** or anti-NP antibody titers of immunized mice were low, 1 plus or minus 0.1 multiply 102. Vaccination with DNA nanospheres was at least as efficient as the gene gun vaccination method. The results suggested that the nanosphere may provide an important new type of DNA vaccine delivery system of particular value in disease states in which a specific immune response phenotype is required. A parallel challenge experiment using the NP antigen given as PowerJect-XR (gene gun) gene gun DNA (3 mu g dose, three total vaccinations) showed a protection level of 80%.

MECHANISM OF ACTION - Cell mediated response stimulation; humoral immune response stimulation.

USE - The nanospheres are used to immunize mammals to raise immune response to antigen (claimed) by cell-mediated and humoral immune responses. They are also used to deliver genes encoding antigens to mammals, to target parenchymal cells of the liver sinusoids, fibroblasts of the connective tissues, cells in the Islets of Langerhans in the pancreas, cardiac myocytes, Chief and parietal cells of the intestine, osteocytes and chondrocytes in bone, keratinocytes, nerve cells of the peripheral nervous system, epithelial cells of the kidney and lung, Sertoli cells of the testis, erythrocytes, leukocytes (monocytes, macrophages, B and T lymphocytes, neutrophils, natural killer cells, progenitor cells, mast cells, eosinophils), platelets and endothelial cells. The nanospheres are used to immunize against HIV and **Ebola** infections.

ADVANTAGE - The nanosphere provides non-viral gene delivery system for delivery of nucleic acids for immunization of animals. Temporal and spatial distribution of cytokines can be altered, thus directing immune response towards a specific immune arm, for example allowing modulating immune response against HIV infection by emphasizing humoral or cellular arm. Coacervate is extracellularly stable. Ligands can be conjugated to nanospheres to stimulate receptor-mediated endocytosis and potentially to target cells/tissues. Lysosomolytic agents can be incorporated to promote escape of intact DNA into cytoplasm. Other bioactive agents (RNA, oligonucleotides, proteins or multiple plasmids) can be co-encapsulated for potential augmentation of immune response through class I

protection from serum nuclease degradation by the matrix and there is little release of nucleic acids until the nanosphere is sequestered into the endolysosomal pathway. There is potential of intracellular sustained release of nucleic acids that may provide more prolonged expression of gene product. Nanosphere is stable in plasma electrolytes and can be lyophilized without loss of bioactivity. Nanospheres can be handled like conventional pharmaceutical formulations in terms of production, reproducibility and storage.

DESCRIPTION OF DRAWING(S) - Survival of mice infected with **Ebola** virus following vaccination with **Ebola** nucleoprotein (NP) pDNA or **Ebola** envelope glycoprotein (**GP**) pDNA delivered by nanosphere. Open square = 0.5 mu g **Ebola** NP pDNA; filled square = 3 mu g **Ebola** NP pDNA; open circle = 0.5 mu g **Ebola GP** pDNA; filled circle = 3 mu g **Ebola** **GP** pDNA; open triangle = 3 mu g control WRG7077 pDNA (vector without the **Ebola** NP or **GP** insert).

5A, 5B/5

L25 ANSWER 29 OF 29 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

Full Text

AN 1999-405117 [34] WPIDS

DNC C1999-119592

TI **Ebola** virus nucleic acid molecules encoding structural proteins.

DC B04 D16

IN NABEL, G J; SANCHEZ, A

PA (NABE-I) NABEL G J; (SANC-I) SANCHEZ A; (USSH) US DEPT HEALTH & HUMAN SERVICES; (UNMI) UNIV MICHIGAN

CYC 31

PI WO 9932147 A1 19990701 (199934)* EN 81
RW: AT BE CH CY DE DK ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: CA JP US
US 6852324 B1 20050208 (200511)
US 2005281844 A1 20051222 (200603)

ADT WO 9932147 A1 WO 1998-US27364 19981223; US 6852324 B1 Provisional US 1997-68655P 19971223, WO 1998-US27364 19981223, US 2001-913909 20010817; US 2005281844 A1 Provisional US 1997-68655P 19971223, Div ex WO 1998-US27364 19981223, Div ex US 2001-913909 20010817, US 2005-38933 20050119

FDT US 6852324 B1 Based on WO 9932147; US 2005281844 A1 Div ex US 6852324

PRAI US 1997-68655P 19971223; US 2001-913909 20010817; US 2005-38933 20050119

AB WO 9932147 A UPAB: 19990825

NOVELTY - A therapeutic composition (A) comprising a nucleic acid molecule encoding an **Ebola** virus structural gene product operatively linked to a control sequence, in a carrier is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) producing a vaccine against disease caused by infection by **Ebola** virus, by:

(a) administering (A) to a test host to determine an amount and frequency of administration to elicit a protective immune response in the host; and

(b) formulating (A) in a form suitable for administration to a treatable host in accordance with the determined amount and frequency of administration;

(2) a vaccine comprising a nucleic acid molecule encoding the transmembrane or secreted form of **Ebola** virus glycoprotein, or **Ebola** virus nucleoprotein, operatively linked to a control sequence, in a carrier.

ACTIVITY - Antiviral.

MECHANISM OF ACTION - Genetic Immunization.

USE - The vaccines are used for immunizing subjects against hemorrhagic fever (claimed). The hemorrhagic fever may be caused by **Ebola** virus or the related **Marburg** virus.

ADVANTAGE - Synthesis of **Ebola** glycoprotein after gene transfer apparently allows more efficient processing and presentation and the generation of immune responses not seen with virus or viral vectors.

DESCRIPTION OF DRAWING(S) - A graph showing immunization with **sGP** or **GP** expression plasmids induces T cell responses to **sGP** in guinea pigs.

Dwg.0/9

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	134.59	249.10

FILE 'MEDLINE' ENTERED AT 10:50:23 ON 06 MAR 2006

FILE LAST UPDATED: 4 MAR 2006 (20060304/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

```
 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s (filovir? or ebola or marburg)
           246 FILOVIR?
           986 EBOLA
          1120 MARBURG
L27       1930 (FILOVIR? OR EBOLA OR MARBURG)

=> s l27 and (env? or glycoprotein? or GP1 or GP2 or sGP or GP)
        413826 ENV?
        167543 GLYCOPROTEIN?
           346 GP1
           233 GP2
           521 SGP
         15219 GP
L28        286 L27 AND (ENV? OR GLYCOPROTEIN? OR GP1 OR GP2 OR SGP OR GP)

=> s l28 and (bivalen? or multivalen?)
          3930 BIVALEN?
          2791 MULTIVALEN?
L29          4 L28 AND (BIVALEN? OR MULTIVALEN?)

=> d l29,ti,1-4

L29  ANSWER 1 OF 4     MEDLINE on STN
TI   Development of a cAdVax-Based Bivalent Ebola Virus Vaccine That
     Induces Immune Responses against both the Sudan and Zaire Species of
     Ebola Virus.

L29  ANSWER 2 OF 4     MEDLINE on STN
TI   Virus-like particles exhibit potential as a pan-filovirus vaccine for
     both Ebola and Marburg viral infections.

L29  ANSWER 3 OF 4     MEDLINE on STN
TI   Glycodendritic structures: promising new antiviral drugs.

L29  ANSWER 4 OF 4     MEDLINE on STN
TI   Individual and bivalent vaccines based on alphavirus replicons protect
     guinea pigs against infection with Lassa and Ebola viruses.


=> d l29,cbib,ab,1,2,4

L29  ANSWER 1 OF 4     MEDLINE on STN
2006114412.    PubMed ID: 16501083.    Development of a cAdVax-Based Bivalent
     Ebola Virus Vaccine That Induces Immune Responses against both the Sudan
     and Zaire Species of Ebola Virus. Wang Danher; Raja Nicholas U; Trubey
     Charles M; Juompan Laure Y; Luo Min; Woraratanadharm Jan; Deitz Stephen B;
     Yu Hong; Swain Benjamin M; Moore Kevin M; Pratt William D; Hart Mary Kate;
     Dong John Y. (GenPhar, Inc., 871 Lowcountry Blvd., Mount Pleasant, SC
     29464.. dongj@genphar.com) . Journal of virology, (2006 Mar) Vol. 80, No.
     6, pp. 2738-46.  Journal code: 0113724. ISSN: 0022-538X. Pub. country:
     United States. Language: English.
AB   Ebola virus (EBOV) causes a severe hemorrhagic fever for which there are
     currently no vaccines or effective treatments.  While lethal human
     outbreaks have so far been restricted to sub-Saharan Africa, the potential
     exploitation of EBOV as a biological weapon cannot be ignored.  Two
     species of EBOV, Sudan ebolavirus (SEBOV) and Zaire ebolavirus (ZEBOV),
     have been responsible for all of the deadly human outbreaks resulting from
     this virus.  Therefore, it is important to develop a vaccine that can
     prevent infection by both lethal species.  Here, we describe the
     bivalent cAdVaxE(GPs/z) vaccine, which includes the SEBOV glycoprotein
     (GP) and ZEBOV GP genes together in a single complex adenovirus-based
     vaccine (cAdVax) vector.  Vaccination of mice with the bivalent
     cAdVaxE(GPs/z) vaccine led to efficient induction of EBOV-specific
     antibody and cell-mediated immune responses to both species of EBOV.  In
     addition, the cAdVax technology demonstrated induction of a 100%
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mice survived challenge with a lethal dose of ZEBOV (30,000 times the 50% lethal dose). This study demonstrates the potential efficacy of a **bivalent** EBOV vaccine based on a cAdVax vaccine vector design.

L29 ANSWER 2 OF 4 MEDLINE on STN
2005180140. PubMed ID: 15811650. Virus-like particles exhibit potential as a pan-**filovirus** vaccine for both **Ebola** and **Marburg** viral infections. Swenson Dana L; Warfield Kelly L; Negley Diane L; Schmaljohn Alan; Aman M Javad; Bavari Sina. (United States Army Medical Research Institute of Infectious Diseases, 1425 Porter Street, Frederick, MD 21702-5011, USA.. dana.swenson@det.amedd.army.mil) . Vaccine, (2005 Apr 27) Vol. 23, No. 23, pp. 3033-42. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.

AB A safe and effective pan-**filovirus** vaccine is highly desirable since the **filoviruses Ebola** virus (EBOV) and **Marburg** virus (MARV) cause highly lethal disease typified by unimpeded viral replication and severe hemorrhagic fever. Previously, we showed that expression of the homologous **glycoprotein** (**GP**) and matrix protein VP40 from a single **filovirus**, either EBOV or MARV, resulted in formation of wild-type virus-like particles (VLPs) in mammalian cells. When used as a vaccine, the wild-type VLPs protected from homologous **filovirus** challenge. The aim of this work was to generate a multi-agent vaccine that would simultaneously protect against multiple and diverse members of the **Filoviridae** family. Our initial approach was to construct hybrid VLPs containing heterologous viral proteins, of EBOV and MARV, and test the efficacy of the hybrid VLPs in a guinea pig model. Our data indicate that vaccination with **GP** was required and sufficient to protect against a homologous **filovirus** challenge, as heterologous wild-type VLPs or hybrid VLPs that did not contain the homologous **GP** failed to protect. Alternately, we vaccinated guinea pigs with a mixture of wild-type **Ebola** and **Marburg** VLPs. Vaccination with a single dose of the **multivalent** VLP vaccine elicited strong immune responses to both viruses and protected animals against EBOV and MARV challenge. This work provides a critical foundation towards the development of a pan-**filovirus** vaccine that is safe and effective for use in primates and humans.

L29 ANSWER 4 OF 4 MEDLINE on STN
2001639983. PubMed ID: 11689649. Individual and **bivalent** vaccines based on alphavirus replicons protect guinea pigs against infection with Lassa and **Ebola** viruses. Pushko P; Geisbert J; Parker M; Jahrling P; Smith J. (Virology Division, United States Army Medical Research Institute for Infectious Diseases, Fort Detrick, Frederick, Maryland 21702, USA.. peter.pushko@amedd.army.mil) . Journal of virology, (2001 Dec) Vol. 75, No. 23, pp. 11677-85. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Lassa and **Ebola** viruses cause acute, often fatal, hemorrhagic fever diseases, for which no effective vaccines are currently available. Although lethal human disease outbreaks have been confined so far to sub-Saharan Africa, they also pose significant epidemiological concern worldwide as demonstrated by several instances of accidental importation of the viruses into North America and Europe. In the present study, we developed experimental individual vaccines for Lassa virus and **bivalent** vaccines for Lassa and **Ebola** viruses that are based on an RNA replicon vector derived from an attenuated strain of Venezuelan equine encephalitis virus. The Lassa and **Ebola** virus genes were expressed from recombinant replicon RNAs that also encoded the replicase function and were capable of efficient intracellular self-amplification. For vaccinations, the recombinant replicons were incorporated into virus-like replicon particles. Guinea pigs vaccinated with particles expressing Lassa virus nucleoprotein or **glycoprotein** genes were protected from lethal challenge with Lassa virus. Vaccination with particles expressing **Ebola** virus **glycoprotein** gene also protected the animals from lethal challenge with **Ebola** virus. In order to evaluate a single vaccine protecting against both Lassa and **Ebola** viruses, we developed dual-expression particles that expressed **glycoprotein** genes of both **Ebola** and Lassa viruses. Vaccination of guinea pigs with either dual-expression particles or with a mixture of particles expressing **Ebola** and Lassa virus **glycoprotein** genes protected the animals against challenges with **Ebola** and Lassa viruses. The results showed that immune responses can be induced against multiple vaccine antigens coexpressed from an alphavirus replicon and suggested the possibility of engineering **multivalent** vaccines based upon alphavirus vectors for arenaviruses, **filoviruses**, and possibly other emerging pathogens.

```
=> d his

     (FILE 'HOME' ENTERED AT 10:36:34 ON 06 MAR 2006)

     FILE 'USPATFULL' ENTERED AT 10:36:47 ON 06 MAR 2006
                E GROGAN C C/IN
L1            1 S E4
```

```
L2            3 S E6
L3            2 S L2 NOT L1
                E SCHMALJOHN A L/IN
L4           12 S E4-E5
L5            9 S L4 AND (FILOVIR? OR MARBURG OR EBOLA)
L6            8 S L5 NOT L1
L7            6 S L6 NOT L2

     FILE 'WPIDS' ENTERED AT 10:39:55 ON 06 MAR 2006
                E GROGAN C C/IN
L8            1 S E3
                E HEVEY M C/IN
L9            2 S E3
L10           1 S L9 NOT L8
                E SCHMALJOHN A L/IN
L11           9 S E2 OR E3
L12           8 S L11 NOT L8
L13           7 S L12 NOT L9
L14           5 S L13 AND (FILOVIR? OR MARBURG OR EBOLA)

     FILE 'MEDLINE' ENTERED AT 10:41:26 ON 06 MAR 2006
                E GROGAN C C/AU
L15           7 S E1 OR E3
                E HEVEY M C/AU
L16          10 S E2-5
L17           0 S L15 AND (FILOVIR? OR EBOLA OR MARBURG)
                E SCHMALJOHN A L/AU
L18          42 S E2-E5
L19          18 S L18 AND (FILOVIR? OR EBOLA OR MARBURG)

     FILE 'USPATFULL' ENTERED AT 10:44:43 ON 06 MAR 2006
L20        2474 S (FILOVIR? OR MARBURG OR EBOLA)
L21         351 S L20 AND (GP1 OR GP2 OR GP OR SGP)
L22          17 S L21 AND (GP1 AND GP2)
L23           9 S L22 AND AY<2003

     FILE 'WPIDS' ENTERED AT 10:47:28 ON 06 MAR 2006
L24         394 S (FILOVIR? OR MARBURG OR EBOLA)
L25          29 S L24 AND (GP1 OR GP2 OR SGP OR GP)
L26           0 S L25 AND (GP?/CLM OR EBOLA/CLM OR MARBURG/CLM)

     FILE 'MEDLINE' ENTERED AT 10:50:23 ON 06 MAR 2006
L27        1930 S (FILOVIR? OR EBOLA OR MARBURG)
L28         286 S L27 AND (ENV? OR GLYCOPROTEIN? OR GP1 OR GP2 OR SGP OR GP)
L29           4 S L28 AND (BIVALEN? OR MULTIVALEN?)

=> s l28 and (GP1 and GP2)
        346 GP1
        233 GP2
L30          11 L28 AND (GP1 AND GP2)

=> s l30 not l29
L31          11 L30 NOT L29

=> d l31,cbib,ab,1-11
```

L31 ANSWER 1 OF 11 MEDLINE on STN
2004251328. PubMed ID: 15103332. Ectodomain shedding of the **glycoprotein GP** of **Ebola** virus. Dolnik Olga; Volchkova Valentina; Garten Wolfgang; Carbonnelle Caroline; Becker Stephan; Kahnt Jorg; Stroher Ute; Klenk Hans-Dieter; Volchkov Viktor. (Institut fur Virologie, Philipps-Universitat Marburg, Marburg, Germany.) The EMBO journal, (2004 May 19) Vol. 23, No. 10, pp. 2175-84. Electronic Publication: 2004-04-22. Journal code: 8208664. ISSN: 0261-4189. Pub. country: England: United Kingdom. Language: English.

AB In this study, release of abundant amounts of the **Ebola** virus (EBOV) surface **glycoprotein GP** in a soluble form from virus-infected cells was investigated. We demonstrate that the mechanism responsible for the release of **GP** is ectodomain shedding mediated by cellular sheddases. Proteolytic cleavage taking place at amino-acid position D637 removes the transmembrane anchor and liberates complexes consisting of **GP1** and truncated **GP2** (**GP**(2delta)) subunits from the cell surface. We show that tumor necrosis factor alpha-converting enzyme (TACE), a member of the ADAM family of zinc-dependent metalloproteases, is involved in EBOV **GP** shedding. This finding shows for the first time that virus-encoded surface **glycoproteins** are substrates for ADAMs. Furthermore, we provide evidence that shed **GP** is present in significant amounts in the blood of virus-infected animals and that it may play an important role in the pathogenesis of infection by efficiently blocking the activity of virus-neutralizing antibodies.

L31 ANSWER 2 OF 11 MEDLINE on STN

ebola virus **glycoprotein** at the single amino acid level by using recombinant vesicular stomatitis viruses. Takada Ayato; Feldmann Heinz; Stroeher Ute; Bray Mike; Watanabe Shinji; Ito Hiroshi; McGregor Martha; Kawaoka Yoshihiro. (Division of Virology, Department of Microbiology and Immunology, Institute of Medical Science, University of Tokyo, Japan.) Journal of virology, (2003 Jan) Vol. 77, No. 2, pp. 1069-74. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB **Ebola** virus causes lethal hemorrhagic fever in humans, but currently there are no effective vaccines or antiviral compounds for this infectious disease. Passive transfer of monoclonal antibodies (MAbs) protects mice from lethal **Ebola** virus infection (J. A. Wilson, M. Hevey, R. Bakken, S. Guest, M. Bray, A. L. Schmaljohn, and M. K. Hart, Science 287:1664-1666, 2000). However, the epitopes responsible for neutralization have been only partially characterized because some of the MAbs do not recognize the short synthetic peptides used for epitope mapping. To identify the amino acids recognized by neutralizing and protective antibodies, we generated a recombinant vesicular stomatitis virus (VSV) containing the **Ebola** virus **glycoprotein**-encoding gene instead of the VSV G protein-encoding gene and used it to select escape variants by growing it in the presence of a MAb (133/3.16 or 226/8.1) that neutralizes the infectivity of the virus. All three variants selected by MAb 133/3.16 contained a single amino acid substitution at amino acid position 549 in the **GP2** subunit. By contrast, MAb 226/8.1 selected three different variants containing substitutions at positions 134, 194, and 199 in the **GP1** subunit, suggesting that this antibody recognized a conformational epitope. Passive transfer of each of these MAbs completely protected mice from a lethal **Ebola** virus infection. These data indicate that neutralizing antibody cocktails for passive prophylaxis and therapy of **Ebola** hemorrhagic fever can reduce the possibility of the emergence of antigenic variants in infected individuals.

L31 ANSWER 3 OF 11 MEDLINE on STN
2001693252. PubMed ID: 11739705. Reverse genetics demonstrates that proteolytic processing of the **Ebola** virus **glycoprotein** is not essential for replication in cell culture. Neumann Gabriele; Feldmann Heinz; Watanabe Shinji; Lukashevich Igor; Kawaoka Yoshihiro. (Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.) Journal of virology, (2002 Jan) Vol. 76, No. 1, pp. 406-10. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB **Ebola** virus, a prime example of an emerging pathogen, causes fatal hemorrhagic fever in humans and in nonhuman primates. Identification of major determinants of **Ebola** virus pathogenicity has been hampered by the lack of effective strategies for experimental mutagenesis. Here we exploit a reverse genetics system that allows the generation of **Ebola** virus from cloned cDNA to engineer a mutant **Ebola** virus with an altered furin recognition motif in the **glycoprotein** (**GP**). When expressed in cells, the **GP** of the wild type, but not of the mutant, virus was cleaved into **GP1** and **GP2**. Although posttranslational furin-mediated cleavage of **GP** was thought to be an essential step in **Ebola** virus infection, generation of a viable mutant **Ebola** virus lacking a furin recognition motif in the **GP** cleavage site demonstrates that **GP** cleavage is not essential for replication of **Ebola** virus in cell culture.

L31 ANSWER 4 OF 11 MEDLINE on STN
2001031466. PubMed ID: 11024148. Functional importance of the coiled-coil of the **Ebola** virus **glycoprotein**. Watanabe S; Takada A; Watanabe T; Ito H; Kida H; Kawaoka Y. (Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.) Journal of virology, (2000 Nov) Vol. 74, No. 21, pp. 10194-201. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB **Ebola** virus contains a single **glycoprotein** (**GP**) that is responsible for receptor binding and membrane fusion and is proteolytically cleaved into disulfide-linked **GP1** and **GP2** subunits. The **GP2** subunit possesses a coiled-coil motif, which plays an important role in the oligomerization and fusion activity of other viral GPs. To determine the functional significance of the coiled-coil motif of **GP2**, we examined the effects of peptides corresponding to the coiled-coil motif of **GP2** on the infectivity of a mutant vesicular stomatitis virus (lacking the receptor-binding/fusion protein) pseudotyped with the **Ebola** virus **GP**. A peptide corresponding to the C-terminal helix reduced the infectivity of the pseudotyped virus. We next introduced alanine substitutions into hydrophobic residues in the coiled-coil motif to identify residues important for **GP** function. None of the substitutions affected **GP** oligomerization, but some mutations, two in the N-terminal helix and all in the C-terminal helix, reduced the ability of **GP** to confer infectivity to the mutant vesicular stomatitis virus without affecting the transport of **GP** to the cell surface, its incorporation into virions, and the production of virus particles. These results indicate that the coiled-coil motif of **GP2** plays an important role in facilitating the

this region could act as efficient antiviral agents.

L31 ANSWER 5 OF 11 MEDLINE on STN
2001021694. PubMed ID: 10950971. Differential induction of cellular detachment by **envelope glycoproteins** of **Marburg** and **Ebola** (Zaire) viruses. Chan S Y; Ma M C; Goldsmith M A. (Gladstone Institute of Virology and Immunology, PO Box 419100, San Francisco, CA 94141-9100, USA.) The Journal of general virology, (2000 Sep) Vol. 81, No. Pt 9, pp. 2155-9. Journal code: 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Human infection by **Marburg** (MBG) or **Ebola** (EBO) virus is associated with fatal haemorrhagic fevers. While these **filoviruses** may both incite disease as a result of explosive virus replication, we hypothesized that expression of individual viral gene products, such as the **envelope glycoprotein** (**GP**), may directly alter target cells and contribute to pathogenesis. We found that expression of EBO **GP** in 293T cells caused significant levels of cellular detachment in the absence of cell death or virus replication. This detachment was induced most potently by membrane-bound EBO **GP**, rather than the shed **glycoprotein** products (**sGP** or **GP1**), and was largely attributable to a domain within the extracellular region of **GP2**. Furthermore, detachment was blocked by the Ser/Thr kinase inhibitor 2-aminopurine, suggesting the importance of a phosphorylation-dependent signalling cascade in inducing detachment. Since MBG **GP** did not induce similar cellular detachment, MBG and EBO **GP** interact with target cells by distinct processes to elicit cellular dysregulation.

L31 ANSWER 6 OF 11 MEDLINE on STN
1999399262. PubMed ID: 10470276. The **glycoproteins** of **Marburg** and **Ebola** virus and their potential roles in pathogenesis. Feldmann H; Volchkov V E; Volchkova V A; Klenk H D. (Institut fur Virologie, Philipps-Universitat Marburg, Germany.) Archives of virology. Supplementum, (1999) Vol. 15, pp. 159-69. Ref: 53. Journal code: 9214275. ISSN: 0939-1983. Pub. country: Austria. Language: English.

AB **Filoviruses** cause systemic infections that can lead to severe hemorrhagic fever in human and non-human primates. The primary target of the virus appears to be the mononuclear phagocytic system. As the virus spreads through the organism, the spectrum of target cells increases to include endothelial cells, fibroblasts, hepatocytes, and many other cells. There is evidence that the **filovirus glycoprotein** plays an important role in cell tropism, spread of infection, and pathogenicity. Biosynthesis of the **glycoprotein** forming the spikes on the virion surface involves cleavage by the host cell protease furin into two disulfide linked subunits **GP1** and **GP2**. **GP1** is also shed in soluble form from infected cells. Different strains of **Ebola** virus show variations in the cleavability of the **glycoprotein,** that may account for differences in pathogenicity, as has been observed with influenza viruses and paramyxoviruses. Expression of the spike **glycoprotein** of **Ebola** virus, but not of **Marburg** virus, requires transcriptional editing. Unedited **GP** mRNA yields the nonstructural **glycoprotein sGP,** which is secreted extensively from infected cells. Whether the soluble **glycoproteins GP1** and **sGP** interfere with the humoral immune response and other defense mechanisms remains to be determined.

L31 ANSWER 7 OF 11 MEDLINE on STN
1999178945. PubMed ID: 10077567. Core structure of the **envelope glycoprotein GP2** from **Ebola** virus at 1.9-A resolution. Malashkevich V N; Schneider B J; McNally M L; Milhollen M A; Pang J X; Kim P S. (Howard Hughes Medical Institute, Whitehead Institute for Biomedical Research, Department of Biology, Massachusetts Institute of Technology, Nine Cambridge Center, Cambridge, MA 02142, USA.) Proceedings of the National Academy of Sciences of the United States of America, (1999 Mar 16) Vol. 96, No. 6, pp. 2662-7. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB **Ebola** virions contain a surface transmembrane **glycoprotein** (**GP**) that is responsible for binding to target cells and subsequent fusion of the viral and host-cell membranes. **GP** is expressed as a single-chain precursor that is posttranslationally processed into the disulfide-linked fragments **GP1** and **GP2**. The **GP2** subunit is thought to mediate membrane fusion. A soluble fragment of the **GP2** ectodomain, lacking the fusion-peptide region and the transmembrane helix, folds into a stable, highly helical structure in aqueous solution. Limited proteolysis studies identify a stable core of the **GP2** ectodomain. This 74-residue core, denoted Ebo-74, was crystallized, and its x-ray structure was determined at 1.9-A resolution. Ebo-74 forms a trimer in which a long, central three-stranded coiled coil is surrounded by shorter C-terminal helices that are packed in an antiparallel orientation into hydrophobic grooves on the surface of the coiled coil. Our results confirm the previously anticipated structural similarity between the **Ebola GP2** ectodomain and the core of the transmembrane subunit from oncogenic retroviruses. The Ebo-74 structure likely represents the fusion-active conformation of the protein, and its overall architecture resembles several other viral

L31 ANSWER 8 OF 11 MEDLINE on STN
1999099033. PubMed ID: 9882347. Endoproteolytic processing of the **ebola** virus **envelope glycoprotein**: cleavage is not required for function. Wool-Lewis R J; Bates P. (Department of Microbiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104-6076, USA.) Journal of virology, (1999 Feb) Vol. 73, No. 2, pp. 1419-26. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Proteolytic processing is required for the activation of numerous viral **glycoproteins**. Here we show that the **envelope glycoprotein** from the Zaire strain of **Ebola** virus (Ebo-**GP**) is proteolytically processed into two subunits, **GP1** and **GP2**, that are likely covalently associated through a disulfide linkage. Murine leukemia virions pseudotyped with Ebo-**GP** contain almost exclusively processed **glycoprotein**, indicating that this is the mature form of Ebo-**GP**. Mutational analysis identified a dibasic motif, reminiscent of furin-like protease processing sites, as the Ebo-**GP** cleavage site. However, analysis of Ebo-**GP** processing in LoVo cells that lack the proprotein convertase furin demonstrated that furin is not required for processing of Ebo-**GP**. In sharp contrast to other viral systems, we found that an uncleaved mutant of Ebo-**GP** was able to mediate infection of various cell lines as efficiently as the wild-type, proteolytically cleaved **glycoprotein**, indicating that cleavage is not required for the activation of Ebo-**GP** despite the conservation of a dibasic cleavage site in all **filoviral envelope glycoproteins**.

L31 ANSWER 9 OF 11 MEDLINE on STN
1998325158. PubMed ID: 9658086. Biochemical analysis of the secreted and virion **glycoproteins** of **Ebola** virus. Sanchez A; Yang Z Y; Xu L; Nabel G J; Crews T; Peters C J. (Special Pathogens Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.. ans1@cdc.gov) . Journal of virology, (1998 Aug) Vol. 72, No. 8, pp. 6442-7. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The **glycoproteins** expressed by a Zaire species of **Ebola** virus were analyzed for cleavage, oligomerization, and other structural properties to better define their functions. The 50- to 70-kDa secreted and 150-kDa virion/structural **glycoproteins** (**SGP** and **GP**, respectively), which share the 295 N-terminal residues, are cleaved near the N terminus by signalase. A second cleavage event, occurring in **GP** at a multibasic site (RRTRR downward arrow) that is likely mediated by furin, results in two **glycoproteins** (**GP1** and **GP2**) linked by disulfide bonding. This furin cleavage site is present in the same position in the GPs of all **Ebola** viruses (R[R/K]X[R/K]R downward arrow), and one is predicted for **Marburg** viruses (R[R/K]KR downward arrow), although in a different location. Based on the results of cross-linking studies, we were able to determine that **Ebola** virion peplomers are composed of trimers of **GP1**-**GP2** heterodimers and that aspects of their structure are similar to those of retroviruses, paramyxoviruses, and influenza viruses. We also determined that **SGP** is secreted from infected cells almost exclusively in the form of a homodimer that is joined by disulfide bonding.

L31 ANSWER 10 OF 11 MEDLINE on STN
1998277077. PubMed ID: 9614872. Release of viral **glycoproteins** during **Ebola** virus infection. Volchkov V E; Volchkova V A; Slenczka W; Klenk H D; Feldmann H. (Institut fur Virologie, Philipps-Universitat Marburg, Germany.. Volchkov@mailer.uni-marburg.de) . Virology, (1998 May 25) Vol. 245, No. 1, pp. 110-9. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB Maturation and release of the **Ebola** virus **glycoprotein GP** were studied in cells infected with either **Ebola** or recombinant vaccinia viruses. Significant amounts of **GP** were found in the culture medium in nonvirion forms. The major form represented the large subunit **GP1** that was shed after release of its disulfide linkage to the smaller transmembrane subunit **GP2**. The minor form were intact **GP1**,2 complexes incorporated into virosomes. Vector-expressed **GP** formed spikes morphologically indistinguishable from spikes on virus particles, indicating that spike assembly is independent of other viral proteins. Analysis of a truncation mutant revealed an early and almost complete release of **GP1**,2 molecules, showing that membrane anchoring is mediated by the carboxy-terminal hydrophobic domain of **GP2**. We have also compared wild-type virus which requires transcriptional editing for synthesis of full-length **GP** with a variant that does not depend on editing. Both viruses released comparable amounts of **GP1**, but the variant expressed only minute amounts of the small, soluble **GP** which is the expression product of nonedited mRNA species of the **GP** gene. The abundant shedding of soluble **GP1** may play an important role in the immunopathology of **Ebola** hemorrhagic fever in experimentally and naturally infected hosts.

1998245155. PubMed ID: 9576958. Processing of the **Ebola** virus **glycoprotein** by the proprotein convertase furin. Volchkov V E; Feldmann H; Volchkova V A; Klenk H D. (Institut fur Virologie, Philipps-Universitat Marburg, 35011 Marburg, Germany.. volchkov@mailer.uni-marburg.de) . Proceedings of the National Academy of Sciences of the United States of America, (1998 May 12) Vol. 95, No. 10, pp. 5762-7. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB In the present study, we have investigated processing and maturation of the **envelope glycoprotein** (**GP**) of **Ebola** virus. When **GP** expressed from vaccinia virus vectors was analyzed by pulse-chase experiments, the mature form and two different precursors were identified. First, the endoplasmic reticulum form preGPer, full-length **GP** with oligomannosidic N-glycans, was detected. preGPer (110 kDa) was replaced by the Golgi-specific form preGP (160 kDa), full-length **GP** containing mature carbohydrates. preGP was finally converted by proteolysis into mature **GP1**,2, which consisted of two disulfide-linked cleavage products, the amino-terminal 140-kDa fragment **GP1**, and the carboxyl-terminal 26-kDa fragment **GP2**. **GP1**,2 was also identified in **Ebola** virions. Studies employing site-directed mutagenesis revealed that **GP** was cleaved at a multibasic amino acid motif located at positions 497 to 501 of the ORF. Cleavage was blocked by a peptidyl chloromethylketone containing such a motif. **GP** is cleaved by the proprotein convertase furin. This was indicated by the observation that cleavage did not occur when **GP** was expressed in furin-defective LoVo cells but that it was restored in these cells by vector-expressed furin. The Reston subtype, which differs from all other **Ebola** viruses by its low human pathogenicity, has a reduced cleavability due to a mutation at the cleavage site. As a result of these observations, it should now be considered that proteolytic processing of **GP** may be an important determinant for the pathogenicity of **Ebola** virus.

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=> d his

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L1            1 S E4
                E HEVEY M C/IN
L2            3 S E6
L3            2 S L2 NOT L1
                E SCHMALJOHN A L/IN
L4           12 S E4-E5
L5            9 S L4 AND (FILOVIR? OR MARBURG OR EBOLA)
L6            8 S L5 NOT L1
L7            6 S L6 NOT L2

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L8            1 S E3
                E HEVEY M C/IN
L9            2 S E3
L10           1 S L9 NOT L8
                E SCHMALJOHN A L/IN
L11           9 S E2 OR E3
L12           8 S L11 NOT L8
L13           7 S L12 NOT L9
L14           5 S L13 AND (FILOVIR? OR MARBURG OR EBOLA)

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L15           7 S E1 OR E3
                E HEVEY M C/AU
L16          10 S E2-5
L17           0 S L15 AND (FILOVIR? OR EBOLA OR MARBURG)
                E SCHMALJOHN A L/AU
L18          42 S E2-E5
L19          18 S L18 AND (FILOVIR? OR EBOLA OR MARBURG)

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L20        2474 S (FILOVIR? OR MARBURG OR EBOLA)
L21         351 S L20 AND (GP1 OR GP2 OR GP OR SGP)
L22          17 S L21 AND (GP1 AND GP2)
L23           9 S L22 AND AY<2003

     FILE 'WPIDS' ENTERED AT 10:47:28 ON 06 MAR 2006
L24         394 S (FILOVIR? OR MARBURG OR EBOLA)
L25          29 S L24 AND (GP1 OR GP2 OR SGP OR GP)
L26           0 S L25 AND (GP?/CLM OR EBOLA/CLM OR MARBURG/CLM)

     FILE 'MEDLINE' ENTERED AT 10:50:23 ON 06 MAR 2006
L27        1930 S (FILOVIR? OR EBOLA OR MARBURG)
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L29           4 S L28 AND (BIVALEN? OR MULTIVALEN?)
L30          11 S L28 AND (GP1 AND GP2)
L31          11 S L30 NOT L29

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        135618 FUSION
       1947979 PROTEIN?
         73102 FUSION PROTEIN?
                 (FUSION(W)PROTEIN?)
L32          23 L28 AND (FUSION PROTEIN?)

=> s l32 not l31
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         58134 GP?/AB
L34          11 L33 AND (GP?/AB)

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L34 ANSWER 1 OF 11 MEDLINE on STN
2004324119. PubMed ID: 15225645. Roles of a conserved proline in the internal fusion peptide of **Ebola glycoprotein**. Gomara Maria J; Mora Puig; Mingarro Ismael; Nieva Jose L. (Unidad de Biofisica (CSIC-UPV/EHU) y Departamento de Bioquimica, Universidad del Pais Vasco, Aptdo. 644, 48080 Bilbao, Spain.) FEBS letters, (2004 Jul 2) Vol. 569, No. 1-3, pp. 261-6. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB The structural determinants underlying the functionality of viral internal fusion peptides (IFPs) are not well understood. We have compared EBOwt (GAAIGLAWIPYFGPAAE), representing the IFP of the **Ebola fusion protein GP,** and EBOwt (GAAIGLAWIPYFGRAAE) derived from a non-functional mutant with conserved Pro537 substituted by Arg. P537R substitution did not abrogate peptide-membrane association, but interfered with the ability to induce bilayer destabilization. Structural determinations suggest that Pro537 is required to preserve a membrane-perturbing local conformation in apolar **environments**.

L34 ANSWER 2 OF 11 MEDLINE on STN
2002481961. PubMed ID: 11208257. The viral transmembrane superfamily: possible divergence of Arenavirus and **Filovirus glycoproteins** from a common RNA virus ancestor. Gallaher W R; DiSimone C; Buchmeier M J. (Department of Microbiology, Immunology & Parasitology, Neuroscience Center of Excellence and Stanley S. Scott Cancer Center, Louisiana State University Medical Center, New Orleans, LA 70112-1393, USA.. wgalla@lsuhsc.edu) . BMC microbiology [electronic resource], (2001) Vol. 1, pp. 1. Electronic Publication: 2001-02-09. Journal code: 100966981. E-ISSN: 1471-2180. Pub. country: England: United Kingdom. Language: English.

AB BACKGROUND: Recent studies of viral entry proteins from influenza, measles, human immunodeficiency virus, type 1 (HIV-1), and **Ebola** virus have shown, first with molecular modeling, and then X-ray crystallographic or other biophysical studies, that these disparate viruses share a coiled-coil type of entry protein. RESULTS: Structural models of the transmembrane **glycoproteins** (**GP**-2) of the Arenaviruses, lymphochoriomeningitis virus (LCMV) and Lassa fever virus, are presented, based on consistent structural propensities despite variation in the amino acid sequence. The principal features of the model, a hydrophobic amino terminus, and two antiparallel helices separated by a glycosylated, antigenic apex, are common to a number of otherwise disparate families of **enveloped** RNA viruses. Within the first amphipathic helix, demonstrable by circular dichroism of a peptide fragment, there is a highly conserved heptad repeat pattern proposed to mediate multimerization by coiled-coil interactions. The amino terminal 18 amino acids are 28% identical and 50% highly similar to the corresponding region of **Ebola,** a member of the **Filovirus** family. Within the second, charged helix just prior to membrane insertion there is also high similarity over the central 18 amino acids in corresponding regions of Lassa and **Ebola,** which may be further related to the similar region of HIV-1 defining a potent antiviral peptide analogue. CONCLUSIONS: These findings indicate a common pattern of structure and function among viral transmembrane **fusion proteins** from a number of virus families. Such a pattern may define a viral transmembrane superfamily that evolved from a common precursor eons ago.

L34 ANSWER 3 OF 11 MEDLINE on STN
2001365983. PubMed ID: 11426696. Virus membrane **fusion proteins**: biological machines that undergo a metamorphosis. Dutch R E; Jardetzky T S; Lamb R A. (Department of Biochemistry, University of Kentucky Medical Center, Lexington 40536, USA.) Bioscience reports, (2000 Dec) Vol. 20, No. 6, pp. 597-612. Ref: 105. Journal code: 8102797. ISSN: 0144-8463. Pub. country: United States. Language: English.

AB **Fusion proteins** from a group of widely disparate viruses, including

retroviral **Env** protein, the **Ebola** virus **Gp**, and the influenza virus haemagglutinin, share a number of common features. All contain multiple glycosylation sites, and must be trimeric and undergo proteolytic cleavage to be fusogenically active. Subsequent to proteolytic cleavage, the subunit containing the transmembrane domain in each case has an extremely hydrophobic region, termed the fusion peptide, or at near its newly generated N-terminus. In addition, all of these viral **fusion proteins** have 4-3 heptad repeat sequences near both the fusion peptide and the transmembrane domain. These regions have been demonstrated from a tight complex, in which the N-terminal heptad repeat forms a trimeric-coiled coil, with the C-terminal heptad repeat forming helical regions that buttress the coiled-coil in an anti-parallel manner. The significance of each of these structural elements in the processing and function of these viral **fusion proteins** is discussed.

L34 ANSWER 4 OF 11 MEDLINE on STN
2000483664. PubMed ID: 11000247. Critical role for the cysteines flanking the internal fusion peptide of avian sarcoma/leukosis virus **envelope glycoprotein**. Delos S E; White J M. (Department of Cell Biology, School of Medicine, University of Virginia Health System, Charlottesville, Virginia 22908, USA.. sed7a@unix.virginia.edu) . Journal of virology, (2000 Oct) Vol. 74, No. 20, pp. 9738-41. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The transmembrane subunit (TM) of the **envelope glycoprotein** (**Env**) of the oncovirus avian sarcoma/leukosis virus (ASLV) contains an internal fusion peptide flanked by two cysteines (C9 and C45). These cysteines, as well as an analogous pair in the **Ebola** virus **GP glycoprotein**, are predicted to be joined by a disulfide bond. To examine the importance of these cysteines, we mutated C9 and C45 in the ASLV subtype A **Env** (**EnvA**), individually and together, to serine. All of the mutant **EnvAs** formed trimers that were composed of the proteolytically processed surface (SU) and TM subunits. All mutant **EnvAs** were incorporated into murine leukemia virus pseudotyped virions and bound receptor with wild-type affinity. Nonetheless, all mutant **EnvAs** were significantly impaired (approximately 1,000-fold) in their ability to support infectivity. They were also significantly impaired in their ability to mediate cell-cell fusion. Our data are consistent with a model in which the internal fusion peptide of ASLV-A **EnvA** exists as a loop that is stabilized by a disulfide bond at its base and in which this stabilized loop serves an important function during virus-cell fusion. The fusion peptide of the **Ebola** virus **GP glycoprotein** may conform to a similar structure.

L34 ANSWER 5 OF 11 MEDLINE on STN
2000056099. PubMed ID: 10588652. A discrete stage of baculovirus GP64-mediated membrane fusion. Kingsley D H; Behbahani A; Rashtian A; Blissard G W; Zimmerberg J. (Laboratory of Cellular and Molecular Biophysics, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 20892-1855, USA.) Molecular biology of the cell, (1999 Dec) Vol. 10, No. 12, pp. 4191-200. Journal code: 9201390. ISSN: 1059-1524. Pub. country: United States. Language: English.

AB Viral **fusion protein** trimers can play a critical role in limiting lipids in membrane fusion. Because the trimeric oligomer of many viral **fusion proteins** is often stabilized by hydrophobic 4-3 heptad repeats, higher-order oligomers might be stabilized by similar sequences. There is a hydrophobic 4-3 heptad repeat contiguous to a putative oligomerization domain of Autographa californica multicapsid nucleopolyhedrovirus **envelope glycoprotein GP64**. We performed mutagenesis and peptide inhibition studies to determine if this sequence might play a role in catalysis of membrane fusion. First, leucine-to-alanine mutants within and flanking the amino terminus of the hydrophobic 4-3 heptad repeat motif that oligomerize into trimers and traffic to insect Sf9 cell surfaces were identified. These mutants retained their wild-type conformation at neutral pH and changed conformation in acidic conditions, as judged by the reactivity of a conformationally sensitive mAb. These mutants, however, were defective for membrane fusion. Second, a peptide encoding the portion flanking the **GP64** hydrophobic 4-3 heptad repeat was synthesized. Adding peptide led to inhibition of membrane fusion, which occurred only when the peptide was present during low pH application. The presence of peptide during low pH application did not prevent low pH-induced conformational changes, as determined by the loss of a conformationally sensitive epitope. In control experiments, a peptide of identical composition but different sequence, or a peptide encoding a portion of the **Ebola GP** heptad motif, had no effect on **GP64**-mediated fusion. Furthermore, when the hemagglutinin (X31 strain) **fusion protein** of influenza was functionally expressed in Sf9 cells, no effect on hemagglutinin-mediated fusion was observed, suggesting that the peptide does not exert nonspecific effects on other **fusion proteins** or cell membranes. Collectively, these studies suggest that the specific peptide sequences of **GP64** that are adjacent to and include portions of the hydrophobic 4-3 heptad repeat play a dynamic role in membrane fusion at a stage that is downstream of the initiation of protein conformational

L34 ANSWER 6 OF 11 MEDLINE on STN
1999412417. PubMed ID: 10482652. Mutational analysis of the putative fusion domain of **Ebola** virus **glycoprotein**. Ito H; Watanabe S; Sanchez A; Whitt M A; Kawaoka Y. (Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.) Journal of virology, (1999 Oct) Vol. 73, No. 10, pp. 8907-12. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB **Ebola** viruses contain a single **glycoprotein** (**GP**) spike, which functions as a receptor binding and membrane **fusion protein**. It contains a highly conserved hydrophobic region (amino acids 524 to 539) located 24 amino acids downstream of the N terminus of the **Ebola** virus **GP2** subunit. Comparison of this region with the structural features of the transmembrane subunit of avian retroviral **GPs** suggests that the conserved **Ebola** virus hydrophobic region may, in fact, serve as the fusion peptide. To test this hypothesis directly, we introduced conservative (alanine) and nonconservative (arginine) amino acid substitutions at eight positions in this region of the **GP2** molecule. The effects of these mutations were deduced from the ability of the **Ebola** virus **GP** to complement the infectivity of a vesicular stomatitis virus (VSV) lacking the receptor-binding G protein. Some mutations, such as Ile-to-Arg substitutions at positions 532 (I532R), F535R, G536A, and P537R, almost completely abolished the ability of the **GP** to support VSV infectivity without affecting the transport of **GP** to the cell surface and its incorporation into virions or the production of virus particles. Other mutations, such as G528R, L529A, L529R, I532A, and F535A, reduced the infectivity of the VSV-**Ebola** virus pseudotypes by at least one-half. These findings, together with previous reports of liposome association with a peptide corresponding to positions 524 to 539 in the **GP** molecule, offer compelling support for a fusion peptide role for the conserved hydrophobic region in the **Ebola** virus **GP**.

L34 ANSWER 7 OF 11 MEDLINE on STN
1999265136. PubMed ID: 10332732. Structural basis for membrane fusion by **enveloped** viruses. Weissenhorn W; Dessen A; Calder L J; Harrison S C; Skehel J J; Wiley D C. (Laboratory of Molecular Medicine, Children's Hospital, Boston, MA 02215, USA.. weissen@embl-grenoble.fr) . Molecular membrane biology, (1999 Jan-Mar) Vol. 16, No. 1, pp. 3-9. Ref: 78. Journal code: 9430797. ISSN: 0968-7688. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **Enveloped** viruses such as HIV-1, influenza virus, and **Ebola** virus express a surface **glycoprotein** that mediates both cell attachment and fusion of viral and cellular membranes. The membrane fusion process leads to the release of viral proteins and the RNA genome into the host cell, initiating an infectious cycle. This review focuses on the HIV-1 **gp41** membrane **fusion protein** and discusses the structural similarities of viral membrane **fusion proteins** from diverse families such as Retroviridae (HIV-1), Orthomyxoviridae (influenza virus), and **Filoviridae** (**Ebola** virus). Their structural organization suggests that they have all evolved to use a similar strategy to promote fusion of viral and cellular membranes. This observation led to the proposal of a general model for viral membrane fusion, which will be discussed in detail.

L34 ANSWER 8 OF 11 MEDLINE on STN
1999036017. PubMed ID: 9820131. Recombinant **Ebola** virus nucleoprotein and **glycoprotein** (Gabon 94 strain) provide new tools for the detection of human infections. Prehaud C; Hellebrand E; Coudrier D; Volchkov V E; Volchkova V A; Feldmann H; Le Guenno B; Bouloy M. (Unite des Arbovirus et virus des Fievres Hemorragiques, Institut Pasteur, Paris, France.) The Journal of general virology, (1998 Nov) Vol. 79 (Pt 11), pp. 2565-72. Journal code: 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB After cloning and sequencing the **glycoprotein** (**GP**) gene of one of the Gabonese strains of **Ebola** virus isolated during the 1994-1996 outbreak, it was shown that the circulating virus was of the Zaire subtype. This was confirmed in this study by cloning and sequencing the nucleoprotein (NP) gene of this strain. These two structural proteins were also expressed as recombinant proteins and used in ELISA tests. NP was expressed as a His-tagged **fusion protein** in Escherichia coli and was purified on resins charged with nickel ions. **GP** was expressed by means of recombinant baculoviruses in Spodoptera frugiperda cells. Both recombinant proteins reacted positively in ELISAs for the detection of IgG antibodies in convalescent human sera from Gabon and Zaire. The difference in the relative titres of anti-NP and -**GP** antibodies was variable, depending on the sera. In addition, the recombinant NP reacted with heterologous sera from Cote d'Ivoire and was used successfully to detect IgM antibodies by mu-capture ELISA in sera from Gabonese patients.

L34 ANSWER 9 OF 11 MEDLINE on STN
1998263303. PubMed ID: 9600912. The central structural feature of the

is a long triple-stranded coiled coil. Weissenhorn W; Calder L J; Wharton S A; Skehel J J; Wiley D C. (Laboratory of Molecular Medicine, Howard Hughes Medical Institute, The Children's Hospital, 320 Longwood Avenue Boston, MA 02215, USA.) Proceedings of the National Academy of Sciences of the United States of America, (1998 May 26) Vol. 95, No. 11, pp. 6032-6. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The ectodomain of the **Ebola** virus **Gp2 glycoprotein** was solubilized with a trimeric, isoleucine zipper derived from GCN4 (pIIGCN4) in place of the hydrophobic fusion peptide at the N terminus. This chimeric molecule forms a trimeric, highly alpha-helical, and very thermostable molecule, as determined by chemical crosslinking and circular dichroism. Electron microscopy indicates that **Gp2** folds into a rod-like structure like influenza HA2 and HIV-1 **gp41**, providing further evidence that viral **fusion proteins** from diverse families such as Orthomyxoviridae (Influenza), Retroviridae (HIV-1), and **Filoviridae** (**Ebola**) share common structural features, and suggesting a common membrane fusion mechanism.

L34 ANSWER 10 OF 11 MEDLINE on STN

1998184553. PubMed ID: 9525641. Characterization of **Ebola** virus entry by using pseudotyped viruses: identification of receptor-deficient cell lines. Wool-Lewis R J; Bates P. (Department of Microbiology, University of Pennsylvania School of Medicine, Philadelphia 19104-6076, USA.) Journal of virology, (1998 Apr) Vol. 72, No. 4, pp. 3155-60. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Studies analyzing **Ebola** virus replication have been severely hampered by the extreme pathogenicity of this virus. To permit analysis of the host range and function of the **Ebola** virus **glycoprotein** (Ebo-**GP**), we have developed a system for pseudotyping these **glycoproteins** into murine leukemia virus (MLV). This pseudotyped virus, MLV(**Ebola**), can be readily concentrated to titers which exceed 5 x 10(6) infectious units/ml and is effectively neutralized by antibodies specific for Ebo-**GP**. Analysis of MLV(**Ebola**) infection revealed that the host range conferred by Ebo-**GP** is very broad, extending to cells of a variety of species. Notably, all lymphoid cell lines tested were completely resistant to infection; we speculate that this is due to the absence of a cellular receptor for Ebo-**GP** on B and T cells. The generation of high-titer MLV(**Ebola**) pseudotypes will be useful for the analysis of immune responses to **Ebola** virus infection, development of neutralizing antibodies, analysis of **glycoprotein** function, and isolation of the cellular receptor(s) for the **Ebola** virus.

L34 ANSWER 11 OF 11 MEDLINE on STN

97076224. PubMed ID: 8918541. Intracellular transport and processing of the **Marburg** virus surface protein in vertebrate and insect cells. Becker S; Klenk H D; Muhlberger E. (Institut fuer Virologie der Philipps-Universitaet-Marburg, Germany.. Becker@mailer.uni.marburg.de) . Virology, (1996 Nov 1) Vol. 225, No. 1, pp. 145-55. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB The surface protein (**GP**) of **Marburg** virus (MBG) is synthesized as a 90-kDa precursor protein which is cotranslationally modified by the addition of high-mannose sugars (140 kDa). This step is followed by the conversion of the N-linked sugars to endoglycosidase H (endo H)-resistant species and the addition of O-linked oliosaccharides leading to a mature protein of 170-200 kDa approximately 30 min after pulse labelling. The mature form of **GP** is efficiently transported to the plasma membrane. **GP** synthesized using the T7 polymerase-driven vaccinia virus expression system was transported with essentially the same kinetics as the authentic **GP**. However, the protein that is shown to appear 30 min after pulse labeling at the plasma membrane was slighly smaller (160 kDa) than **GP** incorporated into the virions (170 kDa). Using a recombinant baculovirus, **GP** was expressed at high levels in insect cells. Three different species could be identified: a 90-kDa unglycosylated **GP** localized in the cytoplasm and two 140-kDa glycosylated proteins. Characterization of the glycosylated **GPs** revealed that processing of the oligosaccharides of **GP** was less efficient in insect cells than in mammalian cells. The majority of **GP** remained endo H sensitive containing high-mannose type N-linked glycans, whereas only a small fraction became endo H resistant carrying processed N-glycans and O-glycans. Tunicamycin treatment of the **GP**-expressing cells demonstrated that N-glycosylation is essential for the transport of the MBG surface protein.

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FILE 'USPATFULL' ENTERED AT 10:36:47 ON 06 MAR 2006

E GROGAN C C/IN

L1 1 S E4

E HEVEY M C/IN

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L3            2 S L2 NOT L1
                E SCHMALJOHN A L/IN
L4           12 S E4-E5
L5            9 S L4 AND (FILOVIR? OR MARBURG OR EBOLA)
L6            8 S L5 NOT L1
L7            6 S L6 NOT L2

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L10           1 S L9 NOT L8
                E SCHMALJOHN A L/IN
L11           9 S E2 OR E3
L12           8 S L11 NOT L8
L13           7 S L12 NOT L9
L14           5 S L13 AND (FILOVIR? OR MARBURG OR EBOLA)

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                E HEVEY M C/AU
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L17           0 S L15 AND (FILOVIR? OR EBOLA OR MARBURG)
                E SCHMALJOHN A L/AU
L18          42 S E2-E5
L19          18 S L18 AND (FILOVIR? OR EBOLA OR MARBURG)

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L20        2474 S (FILOVIR? OR MARBURG OR EBOLA)
L21         351 S L20 AND (GP1 OR GP2 OR GP OR SGP)
L22          17 S L21 AND (GP1 AND GP2)
L23           9 S L22 AND AY<2003

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L24         394 S (FILOVIR? OR MARBURG OR EBOLA)
L25          29 S L24 AND (GP1 OR GP2 OR SGP OR GP)
L26           0 S L25 AND (GP?/CLM OR EBOLA/CLM OR MARBURG/CLM)

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L28         286 S L27 AND (ENV? OR GLYCOPROTEIN? OR GP1 OR GP2 OR SGP OR GP)
L29           4 S L28 AND (BIVALEN? OR MULTIVALEN?)
L30          11 S L28 AND (GP1 AND GP2)
L31          11 S L30 NOT L29
L32          23 S L28 AND (FUSION PROTEIN?)
L33          21 S L32 NOT L31
L34          11 S L33 AND (GP?/AB)

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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
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